

ON THE PATHOLOGICAL ANATOMY OF MULTIPLE  
LYMPHOSARCOMA AND ITS STATUS WITH  
RELATION TO HODGKIN'S DISEASE

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## ON THE PATHOLOGICAL ANATOMY OF MULTIPLE LYMPHOSARCOMA AND ITS STATUS WITH RELATION TO HODGKIN'S DISEASE.

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ALL papers on such diseased conditions as are mentioned in this title begin with the complaint that confusion reigns on account of the employment of a variety of names for the same condition, and the same name for different conditions. The confusion really depends, however, upon our ignorance of the etiology of any of these disturbances, for from the even more confused conglomeration that once formed the group some things have been easily and certainly separated by the recognition of the causative factor. Scrofulous glands, for example, no longer offer the least difficulties in classification, for we know that they are the expression of the activity of the tubercle bacillus, and it is safe to say that similar clear light will be thrown on the remaining confused diseases when the inciting cause of each is discovered. At present, however, there are several diseased states in which tumor-like masses appear, usually arising from the lymph glands or lymphoid tissue elsewhere, of which the cause is quite unknown to us. To such states the names of Hodgkin's disease or pseudoleukemia, lymphosarcoma, lymphoma, chloroma, and myeloma have been applied. Round-cell sarcoma and the various forms of leukemia are also sometimes difficult to distinguish sharply from the rest, and it is indeed only by the study of the mode of growth and distribution of the lesions, supplemented by the minute investigation of the histological changes, that it is possible to subdivide these cases fairly well. It must be said, however, that in any large material there occur cases of which

it is extremely difficult to say certainly into which group they belong, or whether they do not actually represent new and independent conditions. Nevertheless, with the aid of the methods mentioned, it is possible to classify most of the cases in somewhat the same way that the systematic botanist classifies plants, and with the pleasing result that new cases falling into one or other class, according to their general clinical and anatomical character and distribution, will be found to correspond also histologically with the other cases already in that class. This, of course, is not the ideal method of classification, and involves some risk of error, but as long as we do not know the etiological factors, it must suffice.

It is far beyond the scope of this paper to discuss such a classification in general, and this is the more readily passed over since the admirable papers of Paltauf<sup>1</sup> and Sternberg<sup>2</sup> are so accessible. What is intended is rather the study of some 25 cases which occurred at autopsy at the Johns Hopkins Hospital, in the hope that it may prove possible to clearly outline the condition known as multiple lymphosarcoma, and distinguish it from Hodgkin's disease on the one hand, and from round-celled sarcoma, lymphocytic leukemia, etc., on the other. This seems the more desirable because, although the distinctions are fairly clear in the papers referred to above, which come from European writers, there seems to be still some confusion in this country, as shown by the paper of H. W. Gibbons,<sup>3</sup> in which it is claimed that after all there is no difference between lymphosarcoma and Hodgkin's disease.

It may be well to review briefly, with the aid of the summaries of Sternberg and Paltauf, the general characters of the conditions with which we have to deal. These are affections either local or generalized of one part or other of the blood-forming organs—that is, of the lymphoid tissue or of the bone-marrow. They may cause changes limited strictly to these tissues and respecting their boundaries, or they may extend or appear in an isolated way in other tissues. There may or may not be alterations in the blood which depend upon the changes in the hemopoietic tissues. In no single

<sup>1</sup> Lubarsch and Ostertag, *Ergebnisse*, iii, 1.

<sup>2</sup> *Ibid.*, ix, 2.

<sup>3</sup> *Amer. Jour. Med. Sci.*, November, 1906.



instance do we possess any information as to the etiology, so that they must be discussed merely from their morphological characters.

Perhaps the simplest alteration is that known as lymphatism, or the status lymphaticus, in which, without changes in the blood, all the lymph glands, lymphoid nodules in the intestine, and indeed all the other lymphoid tissue in the body, become increased in bulk by an increase in the number of lymphoid cells and in the size of the germinal centres. In this condition there is no question of an invasion of the adjacent tissue, and the capsules of the lymph glands are intact, although stretched. Whether this differs in any essential way from the so-called aleukemic lymphoma mentioned by Paltauf it is difficult to say. Good descriptions of this condition have been given by Blumer, Friedjung, and others. When some portion, if not all, of the lymphoid tissue is stimulated to the great production of new lymphoid cells, there occurs an increase in the bulk of that tissue. This may apparently occur anywhere in the widespread system of lymphoid tissues, even in the bone-marrow. According to Sternberg, there may be enlargement of lymph glands, accumulation of lymphoid cells in unusual tissues, as in the liver, skin, etc., but with no alteration of the morphology of the blood, and this state he describes as pseudoleukemia, a condition that anatomically and histologically completely resembles lymphatic leukemia, but differs from it in the condition of the blood. However accurate the terminology may be from an etymological point of view, it seems unfortunate that this name should be used in this way, since it has been so long and so generally used to express the condition commonly known in this country as Hodgkin's disease.

According to Pappenheim, the changes which we know as lymphatic leukemia arise only when the affection of the lymphoid tissue involves also the bone-marrow; then the cells are swept in great numbers into the blood, and the symptom leukemia is produced. There may, however, be changes of a similar sort, if not quite the same, in the bone-marrow without the production of any leukemia.

Thus, in all the conditions so far described, there is for some reason an increase in the bulk of the lymphoid tissue, due to their rapid proliferation of the lymphoid cells wherever they normally

occur, sometimes rendering them conspicuous where they are normally hardly to be noticed; but such tissue does not pass its boundaries and invade the remaining tissues, and it is only in the cases associated with actual leukemia that the capillaries of the organs are found filled with lymphoid cells.

The mixed-cell leukemias are so easily distinguished from the group of diseases here considered that they need not be dwelt upon further than to state that there we have essentially an affection of the bone-marrow, although the view is rapidly gaining ground that myelocytes and other elements of the myeloid tissue may actually be produced in the spleen and elsewhere in such cases.

Now, Sternberg describes a series of cases in which the blood picture is exactly that of a lymphatic leukemia, except, perhaps, in the fact that the predominant cells are large, mononuclear leukocytes, and in which the changes in the tissues are precisely those of a lymphatic leukemia, except in the one important point that somewhere the proliferating tissue breaks out of the bounds of the lymph glands and invades the adjacent tissue in the way described later for the lymphosarcomata. Such a condition he calls leukosarcomatosis.

Another fairly sharply outlined group is distinguished chiefly by its peculiar pigmentation, the so-called chloroma, in which there are two forms, the first arising from the lymphoid tissue and forming tumors which invade, allows the passage into the blood of abundant large mononuclear cells. It thus resembles precisely the leukosarcomatosis, with the exception of the peculiar green staining, which distinguishes it. The second form arises from the bone-marrow, the tumors consist of myelocytes which are stained green, and which are swept into the blood. Only three cases of this condition have been observed.

The group of myelomata is one difficult to outline exactly, but it should consist of those cases in which tumors, arising from the bone-marrow, in several places simultaneously, are formed of cells which are not granular, as the myelocytes, but are apparently identical with the non-granular forerunners of the myelocytes. (MacCallum, *Jour. Exp. Med.*, vol. vi.) Much dispute has arisen as to



their exact nature, some authors regarding them as plasma cells. The tumors invade but do not metastasize, and there are no characteristic alterations of the blood.

Finally, there are two other great groups in which the lymphoid tissue is preëminently affected, and these form the subject proper of this paper, the so-called Hodgkin's disease and the lymphosarcoma. 9 cases of Hodgkin's disease studied at autopsy form our series, of which 3 were reported by Dr. Dorothy Reed, in her paper on the subject (J. H. H. Reports, vol. x). They are practically identical in their characters, and I can differ in no way from her conclusions as to their histological characters and general relations, but for the sake of comparison will record the cases. Since her paper appeared there have been further studies of the disease by Longcope, Chiari, Benda, Sternberg, and others, in which these authors agree with her histological descriptions, but in some cases, notably in the case of Sternberg, differ in the view held as to the relationship to tuberculosis. In the laboratory of the Johns Hopkins University we have repeatedly inoculated portions of the glands showing the typical lesion into guinea-pigs without producing any tuberculosis, and have concluded that the tuberculosis which is present in some of the cases is merely a concomitant terminal affection. Longcope has confirmed this view in his series of cases, but Sternberg goes so far as to describe the cases without much question as due to the tubercle bacillus, and heads his chapter on the subject, "Eigenartige unter dem Bilde der Pseudoleukämie verlaufende Tuberkulose des lymphatischen Apparates."

The affection is primarily one of the lymph glands, often beginning in the neck, where great enlargement of the cervical glands may result, especially in the supraclavicular region; axillary and inguinal and other glands are often affected. They are usually discrete and show no tendency to become conglomerated or matted together; but sometimes this occurs, and a sort of tumor-like growth results. Abdominal and thoracic lymph glands are soon involved, but there may be a distinct difference in the age of the lesion in different glands. They are on section rather translucent, dull, grayish-white, moist, and homogeneous in appearance when the involvement is

recent, as time progresses they become harder and denser, with streaks and lines of opacity not seen in the fresher glands. Actual necroses sometimes occur. Other organs than the lymph glands may be involved, especially the spleen, liver, and lungs. In none of our cases have the kidneys been involved.

Dr. Reed describes the metastases in the viscera as being of various size, from pinpoint to large nodules. They are usually of grayish-white color, and sharply marked off from the surrounding tissue by an irregular outline. The spleen is sometimes greatly enlarged, and on section may be seen to be thickly studded with the irregular masses of grayish tissue. These masses do not project from the cut surface, but appear to be of about the same consistency as the spleen. Recently two cases have come into our hands in which the lungs were invaded apparently by an extension from the bronchial glands. In one of these cases enormous bronchial glands lay at the bifurcation of the trachea and projected into its lumen through the wall. In both lungs there were dozens of nodules, some enormous, while others were quite minute. In the other case there was a very diffuse invasion of the lung, nodules of translucent appearance occupying the greater portion of the lung and leaving only small areas of lung tissue between them. The pleura was thickened into a translucent layer of tissue, 5 or 6 mm. thick.

In these cases histological examination reveals a tissue always of precisely similar character, so that from the extirpation and microscopic study of a gland the diagnosis can be arrived at with great certainty. There is, as Dr. Reed has emphasized, some variation in the appearance in different stages of the process, but this variation consists merely in differences in the relative quantities of cellular and fibrous tissue.

In the earlier stages the connective-tissue stroma is not very dense. It is, however, much more abundant than the normal reticulum of the gland, whose structure is obliterated by the new-growth, so that the tissue can scarcely be recognized as that of a lymph gland. Only in the earliest stages, for a description of which Reed's and Longcope's papers may be referred to, can the architecture of the gland be made out.



In the meshes of this tissue and more or less coherent with it are great numbers of lymphoid cells, which make up the bulk of the cellular tissue. These are similar in every respect to those normally seen in the lymph gland, except that they are sometimes rather irregular in form and show a somewhat elongated nucleus; with the advance in the age of the process the lymphoid cells become less numerous and the gland more fibrous. Scattered among these cells are many much larger cells, with irregular, ragged cell body, composed of indefinitely granular protoplasm and with a large, sharply outlined, vesicular nucleus. Sometimes this is quite round, more often kidney-shaped or slightly indented, and frequently there are several, as if the main nucleus had given rise to other smaller ones, by a process of budding. Each nucleus has a definite, deeply stained nucleolus, and a number of chromatin granules about its margin. In many cases, but not in all, there are also numerous eosinophile cells with single or lobulated nucleus. These are scattered irregularly, often in great profusion, in certain parts of the gland, and sometimes very abundantly in its capsule. Large, multinucleated giant cells occur but rarely, but are sometimes seen. The later stages differ only in the smaller number of the cellular elements, and the predominance of the fibrous tissue. The nodules scattered in the lung tissue, or in the liver or spleen, present precisely the same characteristics. This tissue sometimes presents areas of necrosis apparently due to insufficient vascularization, while in certain cases, as mentioned above, there is a terminal infection with the tubercle bacillus, in which case characteristic tuberculous lesions may be grafted on the lesions of Hodgkin's disease. Undoubtedly this tissue change is such as cannot be mistaken for any of those already mentioned. It has nothing in common with recognized lesions produced by the tubercle bacillus and pieces of the tissue, except from those cases in which there is an obvious secondary tuberculosis when implanted in the tissues of a guinea-pig, give rise to no tuberculosis. We cannot, therefore, agree with Sternberg and others who regard Hodgkin's disease as merely a peculiar form of tuberculosis. Its distribution is fairly characteristic also, for while the lymph glands, liver, spleen, and, rarely, the lungs, are involved, the kidneys, adrenals, pancreas, digestive tract, bone-

marrow, etc., seem to escape entirely, contrasting in that way with the lymphosarcoma, to be described later.

The cases in our series, not reported by Dr. Reed in her paper, may be briefly recorded as follows:

Elisha C., aged fifty-four years. (Autopsy No. 492; medical No. 3618.) Complains of general pain and cough. Family and personal history unimportant. Has been ill for one year; has not worked for one month. Enlargement of glands in neck for about one year. Red corpuscles, 4,200,000; leukocytes, 4000. The glands on the left side of the neck above the clavicle are enlarged. The glands in left axilla are also enlarged. There is a rupial crust on left upper arm. The inguinal glands somewhat enlarged; epitrochlears not palpable. Diagnosis of syphilis made. Blood count, five days before his death, was 4,320,000; leukocytes, 6000; hemoglobin, 29 per cent.

*Anatomical Diagnosis.* Hodgkin's disease; sarcoma of axillary, supra-clavicular, retroperitoneal, and inguinal glands, spleen and liver; rupia on left arm; general streptococcus infection. On left side of neck, from the ear to the clavicle, a lobulated mass of enlarged glands.

*Heart and lungs* negative.

*Spleen* enlarged and covered with fibrin; everywhere mottled on surface and on section with white, firm, opaque areas, the largest the size of a pea. These show no tendency to softening. Splenic substance between these is purple and less firm than the nodules.

*Liver* shows many opaque nodules, indistinctly outlined, often surrounded by a hemorrhagic zone of congested liver substance. These are more abundant in right lobe.

*Kidneys* pale; otherwise normal.

*Lymph Glands.* Those above the clavicle form a continuous mass of more or less discrete, separable, enlarged glands. Axillary and retroperitoneal glands are also enlarged, but not so greatly as in the cervical region, where they reach the size of a pigeon's egg. Gastrohepatic and pyloric glands enlarged. Inguinal glands and one in the right inguinal fossa enlarged. On section, the glands are semitranslucent, yellowish in color, with areas of varying sizes; opaque as compared with the surroundings; glands rather soft. On section the lymph glands show microscopically that the tissue is replaced by an altered tissue composed of small, rounded, and epithelial cells, interspersed with large cells with large, budding vesicular nucleus. Eosinophile cells are not abundant, but do occur. The whole reproduces fairly the picture of Hodgkin's disease. The tissue in the spleen and other involved glands is identical.

David F. H., aged twenty-seven years; white. (Autopsy No. 566.) Patient admitted on August 9, 1894. Complains of being generally worn out. Letter from Dr. Wolfe says patient has been sick for six months, and that on February



1, 1894, he removed a bunch of twenty-five glands from the left axilla, the nature of which he did not know.

*Family and past history* have no bearing on case.

*Present History.* Illness began six months ago, when he gave up work; has some pain in abdomen; dull headache; appetite variable; bowels irregular; nose bleed on one or two occasions; irregular chills; no swelling of legs or ankles, but some pain in legs.

*Physical Examination.* Was practically negative; one large tender gland on right side of neck. Spleen normal; liver palpable.

*Blood examination* was negative, except for an anemia.

*Anatomical Diagnosis.* Hodgkin's disease; enlargement of axillary, bronchial, pericardial, tracheal, anterior, and posterior mediastinal retroperitoneal, gastrohepatic, and peripancreatic glands; nodules in spleen and liver; jaundice; ascites; and hydrothorax.

Peritoneal cavity contains 450 c.c. of bile-stained fluid. Liver extends  $6\frac{1}{2}$  cm. below the costal margin. Retroperitoneal glands are enlarged, but the mesenteric are not larger than normal.

Pleural cavities contain 50 to 100 c.c. of bile-stained fluid, respectively.

*Heart and lungs* show no abnormality.

Bronchial and anterior mediastinal glands are much enlarged, and on section are seen to be partly occupied by a new tissue of grayish-red color, which is necrotic in places.

The necrotic areas are especially deeply bile-stained.

*Liver* weighs 2350 grams; its surface is roughened by numerous large and small nodules, which vary in color from grayish white to yellowish red. They measure 5 x 3 cm. in some cases, but most of them are not more than 1 to 2 mm. in diameter, while some are very minute.

There are three or four of the large nodules which are found both in the right and left lobe. The nodules are sharply outlined and frequently contain necrotic areas. The intervening liver tissue is dark in color and edematous. The gastrohepatic glands are enlarged from the presence of nodules of the new tissue.

*Spleen* weighs 450 grams and measures 14 x 7 x 4 cm. Through the capsule and on section there are seen many nodules resembling those seen in the liver. The largest of these do not exceed 1 cm. in diameter. They are generally surrounded by a zone of hemorrhage or congestion, and the intervening spleen is dark purplish red in color. The centres of many of the nodules are necrotic.

*Kidneys and pancreas* are apparently normal, but there is a mass of enlarged glands closely attached to the pancreas.

*Intestinal tract* is normal.

*Retroperitoneal glands* are enlarged throughout, enclosing the aorta in a mass which extends into the pelvis. The largest of these glands is about the size of a



pigeon's egg. The left axillary glands are much enlarged, but discrete; right axillary glands not enlarged; nor were the inguinal glands.

*Microscopically*, the newly formed tissue is found to be alike in all situations. It is a dense, coherent tissue, formed of elongated fibroblast-like cells, which are bound together into a firm structure. In the meshes of this lie many cells of the character of lymphoid cells. These are very numerous, but distinct eosinophile cells are not seen. There are also many large cells with large vesicular nuclei, with distinct nucleolus. There are often several such nuclei. The protoplasm is abundant and slightly granular, but there are no specific granulations.

The liver shows this tissue in circumscribed areas surrounded by compressed liver tissue. Necrosis is common in these patches, which lie chiefly about the portal vessels, but occur also elsewhere.

Numerous necroses occur in the lymph glands, which are entirely replaced by the new tissue.

The spleen contains infiltrating masses of the same tissue, which, however, are not to be easily outlined, as the cells seem to wander off among the normal elements of the spleen. Large areas of necrosis exist here also.

Josephine B., aged thirty-two years; white; March 16, 1895. (Medical No. 4772. Autopsy No. 741.) Present illness began six months ago. Complains of general weakness. The posterior cervical glands enlarged. Red corpuscles, 3,160,000; leukocytes, 6000. No glands other than cervical are enlarged. The patient shows a series of curious elevations of temperature, each lasting about one week, and then returning to normal or subnormal. In the latter part of the illness the attacks of fever lasted longer. Before the death of the patient the red corpuscles ran to 1,132,000, and leukocytes to 1000. The spleen became palpable; evidently the lymph glands are not enormously enlarged.

*Anatomical Diagnosis.* Hodgkin's disease, with involvement of the liver, spleen, cervical, axillary, inguinal, retroperitoneal, and mesenteric glands; bronchopneumonia; cirrhosis of liver, etc.

*Heart* shows no abnormality.

*Lungs*, except for the lobular areas of pneumonic consolidation, show no especial changes.

*Spleen* is enlarged, weighing 1030 grams, measuring 21 x 13.5 x 7 cm. Scattered through the substance and shining through the capsule are numerous whitish nodules of tissue different from that of the spleen. These measure 1 to 10 mm. in diameter, and are usually rounded and sharply outlined against the soft, dark-brownish, splenic pulp. The nodules are yellowish white in color, but present foci of necrosis, the central portions sometimes being dark red in color. The Malpighian bodies can be easily distinguished by their gray, translucent appearance.

*Liver* weighs 2150 grams. The surface of the liver, as well as the cut surface, is roughened by projecting nodules of liver tissue. There are a few yellowish-white nodules scattered through the liver, similar to those seen in the spleen.

*Kidneys, pancreas, adrenals, digestive tract, etc.*, seem normal.

*Bone-marrow* of the femur is dark red.

*Lymph glands* on both sides of the neck are enlarged, but discrete. They reach the size of a walnut and are firm and freely movable upon each other, their capsules being unaffected. On section they are grayish-white, but show small, opaque areas of necrosis. Axillary, inguinal, retroperitoneal, and mesenteric glands are similarly altered, but to a less extent.

*Microscopic examination* of the new tissue which occurs in the glands, spleen, and liver shows it to be made up of a fairly dense stroma, in the meshes of which lies cells with rather elongated fibroblast-like nucleus, together with many smaller cells of lymphoid character. There are also many large cells with large vesicular nucleus, very rich in chromatin. These are somewhat rounded and fairly sharply outlined, and their nucleus is rounded or indented, sometimes appearing as if in process of budding. The chromatin particles are very dense and stain very deeply. There are no specific granulations in the protoplasm. No eosinophile cells are to be seen.

The patches of foreign tissue in the spleen and liver prove to have the same characters.

Mrs. A. B., aged thirty-two years; admitted May 2, 1902; died, 1904. Complained of swollen glands on left side of neck and arm. Personal history good. In November, 1901, first noticed gland below the left arm. These have gradually enlarged. Patient has lost in weight; is fairly well nourished. Several hard, movable glands palpable in left axilla. Just above the clavicle and posterior to the sternomastoid muscle is a group of enlarged glands. Red corpuscles, 4,128,000; leukocytes, 11,000. The glands dissected away May 3, 1902. A mass of glands being removed from the left side of the neck. A section of the gland removed reported upon as follows: Normal distinction between follicles and sinuses is lost. Capsule thickened and infiltrated with small round cells. Reticulum separating the cells is increased in thickness. The cells are a mixture of lymphoid and epithelioid cells, with occasional large cells, containing two or three nuclei. Eosinophiles are scarce. Patient discharged after operation. Died some time later.

*Autopsy.* December, 1903. (Autopsy No. 2220.)

*Anatomical Diagnosis.* Hodgkin's disease, involving cervical, bronchial, mediastinal, and retroperitoneal lymph glands; invasion of the anterior mediastinum, trachea, and both lungs.

Only the thoracic and abdominal organs were sent to the laboratory. There are nodules along the posterior surface of the sternum in the anterior mediastinum, and posterior cervical lymph glands. The inguinal glands were not involved. The axillary glands had been involved and were removed at operation. In the anterior mediastinal tissue there is a large tumor mass, which surrounds the trachea and invades its lumen just above the bifurcation. The bronchi are not encroached upon, but the bronchial glands at the bifurcation and



at the hilum of each lung are enormously enlarged. From these there extend lobulated masses, of a soft, white, tumor growth, into the substance of the lungs, forming great masses in each lung. Smaller nodules are scattered throughout the lung substance, and appear on the surface. The lung in the neighborhood is edematous, somewhat compressed, shows opaque, yellow dots. The spleen is enlarged and soft, and velvety in appearance. On section, contains no tumor nodules. The retroperitoneal glands are enlarged and completely replaced by the tumor tissue.

The microscopic character of glands, extirpated at operation, in this case, has been described by Longcope (*Bull. of the Ayer Clinical Laboratory*, October, 1903, No. 1), and the lesions found at autopsy agree well with what he has written.

The lymph glands show none of their normal architecture, the sinuses and lymph cords being obliterated by the solid mass of new tissue, which here does not respect the capsules of the gland, but infiltrates through it. The tissue has a fairly dense stroma, and as far as its cellular structure is concerned, corresponds exactly with Dr. Reed's description. The lymphoid cells are not associated with many eosinophile cells, but the large cells with large vesicular nucleus or nuclei are very abundant and characteristic.

Of especial interest are the nodules in the lung where the process of growth may be looked upon as rather different from that seen in the glands, inasmuch as it is advancing into a tissue not of lymphatic type. The smaller nodules show this process best, and there the nodule is found surrounded by somewhat compressed alveoli, but including also within its substance many alveoli which have become collapsed and in which the desquamated epithelium is still to be seen. The stroma of the new tissue is here particularly delicate and spread out so that the cells, which lie in its meshes, are not crowded together, but stand rather far apart. Possibly some of the alveoli may be entered by the new tissue, but one gets the impression that they are merely separated and collapsed by the new-growth of tissue in their walls.

Ralph L., aged fifteen years; colored; admitted June 15, 1904. (Medical No. 17223.) Previous history good. Last August became weak and easily exhausted. For four months had enlarged inguinal glands on left side. During the past winter had slight cough with mucous expectoration. The glands in the neck and axillæ also enlarged. At present all the glands are greatly enlarged. The axillary and pectoral glands being matted together in large masses. Percussion note is absolutely flat over the entire right lung. Spleen markedly enlarged. Red corpuscles, 2,950,000; leukocytes, 10,600; no tubercle bacilli found in the sputum. Differential count: Polymorphonuclears, 64 per cent.; small mononuclears, 30 per cent.; large mononuclears, 5.3 per cent.; eosinophiles, 0.3 per cent.; myelocytes, 0.3 per cent. The right side is practically immovable, with harsh tubular breathing heard over the lung, with coarse, dry rales. Under arsenic the glands have diminished in size. Patient died July 18.



The gland extirpated, June 22, the following note was made upon its microscopic appearance. The gland is much enlarged and has lost its normal architecture almost completely. One cannot any longer distinguish lymph sinuses and lymph cords; the tissue is homogeneous in appearance. A few minute areas of coagulative necrosis being found. These have no appearance of being tuberculous. There is a fairly abundant connective-tissue stroma in the meshes of which the cells are chiefly of the lymphoid type. There are, however, numerous large cells with sharply outlined vesicular nucleus, and a deeply staining nucleolus. These have a somewhat irregular ragged protoplasm; many of them have two or more nuclei; some are found in mitosis. Eosinophile cells are not present in any number.

*Diagnosis* of Hodgkin's disease made from this gland.

*Autopsy*, 4 P.M., July 19, 1904. (Autopsy No. 2351.)

*Anatomical Diagnosis.* Hodgkin's disease; general involvement of lymph glands, liver, right lung, and spleen.

*Body* is that of an emaciated colored boy, 155 cm. in length. The superficial lymph glands are all enlarged; cervical, axillary, epitrochlear, and inguinal. The peritoneal cavity contains a little clear fluid. The right pleural cavity is obliterated by adhesions.

*Heart* is practically normal.

*Lungs.* The left lung is normal. The bronchial glands are enlarged to a diameter of 2 cm. The right lung is adherent to the chest wall and diaphragm. The bronchial lymph glands are enlarged and discrete, reaching a diameter of 3 cm. The lung feels quite solid, and weighs about 1500 grams. On section, the pleura averages 5 mm. in thickness; has a white fibrous edematous appearance, in which small bloodvessels are seen. The cut surface of the lung shows the lung tissue to have been replaced to a large extent by firm, grayish translucent nodules, from 1 to 4 mm. in diameter, separated by the compressed lung tissue, which has a pinkish-yellow color, and is very opaque. Small hemorrhages in the lung tissue, combined with this opacity, to give the entire surface a variegated appearance. The nodules do not bulge from the surface.

*Spleen* is large and firm; measures 15x10x4 cm. Surface is smooth. Cut surface is dry and of bright-red color, with a grayish mottling. The Malpighian bodies, trabeculae, and vessels are prominent.

*Kidneys, liver, pancreas, stomach, and intestines* show no special abnormality. The lymph glands are everywhere enlarged, the retroperitoneal being the largest, some of them measuring about 4 cm. in length by 2 cm. in diameter. These large lymph glands are rather firm and elastic, and on section present an opaque, white, glistening surface, mottled with yellowish areas. Most of the glands, however, are pinkish gray in color.

While the diagnosis of Hodgkin's disease seems justifiable in this case after the microscopic examination of the tissue, the tissues present such an extraordinary appearance that objections to this diagnosis might well occur. Every-

where the connective-tissue growth is the predominant feature of the lesion. As described above, the lymph glands were elastic and firm in the fresh state, and the lung was rendered very dense and elastic by the presence of smooth, firm nodules throughout it. Corresponding with this the lymph nodes are found to be replaced by a tissue which is almost entirely fibrous tissue, which takes a deep, pink stain. Lymphoid cells are scattered sparsely through it. Eosinophile cells are rare, and the large cells with vesicular nuclei are almost lacking. Still there are areas pretty thickly scattered through this fibrous tissue, in which these cells do occur in little groups, and are there surrounded by closely arranged lymphoid cells; sometimes with eosinophile cells also. Such foci of cellular tissue have quite the character of the tissue described in the other cases, and from them the diagnosis seems possible.

In the lung the same thing is true. The nodules are composed chiefly of a loose, fibrous tissue, made up of fibroblast-like cells, joined together by their long, wavy processes and relatively poor in lymphoid cells. Such tissue penetrates between the air cells, which are seen widely separated and collapsed, their fatty epithelium compressed together in the flattened lumen. Here, too, however, there are in places foci of densely cellular tissue which contains all the types of cells seen in other cases. It seems probable, therefore, that this is really a case of Hodgkin's disease, although it is true that the mode of growth and the character of the tissue are peculiar.

There remain to be described certain other cases in which tumor-like masses occur composed largely of cells resembling lymphoid cells, but without definite alterations of the blood. Eight of these cases, which were studied at autopsy in our laboratory, were found to correspond with Kundrat's description of lymphosarcoma, while the rest must be regarded as true round-cell sarcomata.

From the literature it is difficult to arrive at any clear conception of the different processes, largely on account of the insufficient histological descriptions, the distribution and blood changes being relied upon almost entirely for their differentiation.

Paltauf, in his review of the literature, is followed by Sternberg, who brings it up to date. It is unnecessary to review all this literature again, especially since most of it is derived from text-books and represents the opinions of their authors; but an idea of its content may be given in a few words.

Virchow separated true sarcoma of the lymph glands from lymphosarcoma, which included the forms of hyperplasia of the glands, some



of which, owing to the presence of large cells, became malignant, and were thus distinguished from the simple lymphoma.

Billroth describes as malignant lymphoma, hyperplastic generalizing tumors of the glands, including sarcomatous tumors of the glands.

V. Winiwarter uses the term lymphosarcoma to mean a sarcoma primary in the lymph gland, while pseudoleukemia and lymphoma include glandular hyperplasia, scrofulous and leukemic tumors, etc. Cohnheim distinguished inflammatory hyperplasia such as tuberculous, leukemic, and pseudoleukemic changes from tumor growth (lymphoma, lymphosarcoma).

Ziegler agrees essentially with v. Winiwarter, while Orth divides these conditions into simple hyperplastic lymphoma, malignant lymphoma (leukemia, lymphosarcoma, malign aleukemic lymphoma) and sarcoma of the lymph glands.

Dreschfeld distinguishes lymphosarcoma, malign lymphoma, and pseudoleukemia (Hodgkin's disease).

Kundrat, in an address on a series of cases which he demonstrated, introduced the new term, lymphosarcomatosis, to indicate a condition which is to be pretty clearly distinguished from true sarcoma and from leukemic manifestations or pseudoleukemia. Paltauf, accepting this suggestion, sets up a classification of all these diseases as follows:

1. Aleukemia lymphoma: (a) simple local regionary lymphoma; (b) pseudoleukemia.

2. Lymphosarcomatosis (Kundrat).

3. Sarcoma (spindle, alveolar, pigmented, round celled, etc.

Sternberg ends his monograph also with a systematic classification of all these diseases, which, in order to show his conception of their relations, I may translate here.

*Primary Diseases of the Lymphatic and Hematopoietic Apparatus.*

- A. Local limited homologous (hyperplastic) tissue growth

- (a) with discharge of the cellular elements into the blood and homologous change of the tissue of the lymphatic and hemopoietic apparatus.



1. Lymphatic apparatus—lymphocytes in blood—*lymphatic leukemia*.
  2. Myeloid tissue myelocytes in blood—*mixed-cell leukemia*,
  - (b) with slight or no discharge of cellular elements in the blood.
  3. Of all lymphatic tissue in diffuse way—*pseudoleukemia*.
  4. Of the lymphatic tissue of bone-marrow in form of a tumor—*lymphatic myeloma*?
  5. Of myeloid tissue of bone-marrow in form of a tumor—*myeloid myeloma*.
- B. Atypical growths invading the neighborhood with heterotopical new-growths:
- (a) With discharge of cellular elements in the blood.
  6. Of the lymphatic tissue—discharge of ungranulated pathological cells—*leukosarcomatosis* or *chloroleukosarcomatosis*.
  7. Of myeloid tissue—discharge of granular pathological cells—*chloromyelosarcomatosis*.
  - (b) Without discharge of cellular elements into the blood.
  8. Of the lymphatic tissue—*lymphosarcomatosis*.

Of all these subdivisions which are here retold for the sake of clearness, that with which Kundrat concerned himself, interests us, especially inasmuch as the eight cases which we have studied at autopsy seem to fall into this group.

Kundrat describes as lymphosarcomatosis a more or less widespread lesion with tumor formation, arising from a lymph gland, or a group of them, or from some lymphoid tissue, such as occurs in the intestinal wall, pharynx, etc. Such a tumor mass is composed of a delicate reticulum, in the meshes of which lie cells rather larger than lymphoid cells. It fails to respect the capsules of the lymph glands, but grows rapidly to invade and infiltrate the adjacent tissues. It is thought that the growth may occur by transportation of the cells by way of the lymph stream, as well as by direct extension and implantation; but in these cases, too, the continuity of the growth can be fairly well established by discovering the involvement of the intervening lymphatic glands, etc. The tumor tends to spread in loose tissue and in film or plate form over serous surfaces.

Metastases in distant organs, explainable only by transportation by the blood stream, are uncommon.

The tumor forms large infiltrating masses in the mediastinum or in the cervical or pharyngeal region, or, in other cases, involves the intestinal wall, where it may cause a diffuse thickening of the wall, with a widening of the intestine at the involved area. In such cases it is not uncommon to find other organs, such as the adrenal and pancreas, practically buried in an infiltrating mass of such tissue. Where the tumor appears in nodular form in such organs as the heart, kidney, etc., the sharply outlined nodule seen with the naked eye proves to be only a fairly localized infiltration, the muscle fibers or tubules being merely separated by infiltrating cells.

The description of our eight cases will show how true Kundrat's observations were, and will show fairly well the obvious distinction to be drawn between this condition and Hodgkin's disease, which we have already mentioned. It is apparent from these eight cases that lymphosarcomata fall readily into two groups: (1) Those which originate in the mediastinal or thoracic tissues and invade the pleura, pericardium, tonsils, pharynx, etc., but leave unaffected the abdominal organs. These are in general composed of smaller cells than the others and contain none of the large phagocytic cells. (2) Those in which the most striking lesion is in the intestinal wall. There were five of these cases with involvement of such organ in addition to the intestine, as the liver, stomach, pancreas, adrenal, thymus, kidneys, testicle, etc. These are composed of rather large cells, with interspersed phagocytic cells. It seems probable, from this distribution, that if it be true that some unknown infectious agent causes this growth, the infection may begin in the one group in the tonsils, pharynx, etc., while in the other case it arises from the intestinal mucosa. The cases are as follows—much condensed from the notes:

CASE I.—John K., aged twenty-seven years; white. (Autopsy No. 22.) Complained of sore throat, swelling of the neck, shortness of breath. The swellings in the lower part of the neck on the left side firm and nodular; not tender; freely movable beneath the skin. The right tonsil much enlarged and ulcerated. Extensive dulness on the right side of the chest from the clavicle downward. The left side normal.



*Anatomical Diagnosis.* Lymphosarcoma of mediastinum and cervical lymph glands of pericardium, myocardium, and pleuræ.

On the left side of the neck, commencing at the clavicle and extending up nearly to the angle of the jaw, there is an irregular, firm swelling composed of several more or less distinct masses. The glands in the axilla and inguinal region not enlarged. In the thorax there is a large tumor mass, irregular in shape, with numerous smooth projections. It extends farther into the right than into the left pleura, pushing the heart to the left side and extending down over the pericardium in front. All of the great cardiac vessels, with the exception of the inferior vena cava, are surrounded by the tumor. The posterior mediastinal glands are converted into a tissue of the same character as the tumor. On section, the tumor is mottled, in general of a grayish color, firm in consistency, although abundant juice could be squeezed out from it. There are numerous points of hemorrhage and here and there large yellow caseous areas, sharply separated from the surrounding tissue. The cervical glands are matted together in a mass like the tumor, internal jugular, carotid, and pneumogastric nerves run over this mass, but are not involved. The right pleural cavity contains 1800 c.c. of clear fluid. The right lung is compressed by the exudate, the lower portion airless. The anterior edge of the lung is adherent to the tumor, which invades the lung slightly. The left lung is free, and air-containing throughout. The right tonsil is greatly enlarged, and on section of the same consistency as the tumor. The pericardium is rough and dull, and over the greater part of its extent covered with slightly projecting tumor masses, especially on the parietal layer. The diaphragm also shows some tumor masses. The mesenteric glands are enlarged; some of them present the appearance of the tumor. The abdominal organs in general show nothing special. Scrapings of the tumor showed nothing but small lymphoid cells, varying slightly in size, with a large nucleus and a small protoplasmic margin. Frozen section showed a very slight amount of stroma. Sections of the heart showed an infiltration of the heart muscle with fat.

Microscopic examination of the tumor shows that it is uniform in character wherever it occurs. It is found to infiltrate into the tissue spreading apart the tissue elements, but not growing in the form of solid nodules. The tumor substance is made up of a very delicate stroma, in the meshes of which lie cells of uniform character; all are rounded, with rather ragged protoplasm and vesicular nucleus provided with a nucleolus. The cells measure 5 to 8 mikra in diameter, the largest not exceeding 9 mm. Mitotic figures are abundant. Some portions of the tumor growth are very compact, while other areas are loose and spread wide apart. Areas of necrosis occur here and there.

The pleural tissue is densely infiltrated with these cells, which outline the fat cells by filling up the space between them.

*Liver, spleen, kidney, and lung* are practically normal on section.



CASE II.—Margaret G., aged twenty-four years; white; single; admitted April 17, died May 8, 1890. (Autopsy No. 92.) Patient has been well, except for an attack of typhoid fever ten years ago, up to one year ago, when she began to have indigestion and pain in epigastrium. Frequent attacks of abdominal pain recently, with vomiting. Patient is very anemic and emaciated. Legs and forearms edematous. A large mass found to fill the entire abdomen, projecting on left side and lying transversely below umbilicus, measuring 32 x 17 cm. The tumor is felt to be hard, rounded, slightly irregular over surface, with a deep notch in upper margin. Tympany over whole abdomen and over the mass, which is not sensitive on pressure. Spleen not enlarged. Urine negative. Temperature ranged about 100° to 101.5°; pulse 120 to 140.

*Autopsy, May 8. Anatomical Diagnosis.* Lymphosarcoma of mesenteric glands; involvement of intestine; volvulus of jejunum, with ulceration into a cavity in the tumor; fatty degeneration of heart, liver, and kidney; acute fibrinous peritonitis.

*Body.* Medium size; intensely anemic. In the peritoneal cavity, a considerable amount, about 800 c.c., of yellowish, slightly opaque fluid. In the median line, a greatly distended portion of the transverse colon appears beneath, and to the left of this is a large, fluctuating tumor mass, into which the small intestine seems to enter.

Further examination of the tumor mass shows that the lower portion of the transverse colon and the whole of the descending colon are adherent to this and pass in part directly beneath it. The upper part of the jejunum passes, apparently, directly into the tumor, and opens directly into a large cavity in the interior of the tumor. The intestine at this point is enormously dilated, its walls thickened and covered with nodular masses. Section of the intestinal wall at the point most affected shows the entire thickness 1 cm., composed of a soft, translucent, gelatinous-looking mass. The nodules projecting into the opening are of the same sort of tissue. The balance of intestinal tract and pancreas normal.

*Kidneys and liver* enlarged and pale.

Suprarenal capsules normal.

*Microscopic Examination.* Sections passing through the various tumor masses show a tissue which is uniform throughout and identical in all situations. The stroma is delicate, although a little more conspicuous than in Case I. Capillary bloodvessels are abundant. The meshes of the stroma are filled with loose cells, which are rounded, with smooth outline and relatively large nucleus. They measure 6 to 12 mm. and average about 8 mm., very exceptional cells measuring 14 mm. They are thus rather larger than the cells in Case I. There are some mitotic figures, although these are somewhat indistinct. The section is not perfectly homogeneous, for there are certain round spaces among the cells which contain large cells with irregular, vacuolated protoplasm, which are phagocytic. These are extremely pale and difficult to outline and are provided

with a large, pale, vesicular nucleus. They measure 12 to 20 mm. in diameter. There are occasional patches of necrosis throughout the sections. That passing through the intestine shows that the mucosa has been destroyed and the submucosa replaced completely by a solid mass of the tumor, which also infiltrates between the fibers of the muscularis. The bloodvessels are distended with red corpuscles, but contain none of the tumor elements.

CASE III.—Peter S., aged twenty-seven years; white. (Autopsy No. 225.) This case has been reported in detail by Dr. Flexner in his paper on "Lymphosarcomata," but is recorded briefly here in order to complete the series.

Man has been well up to present illness, which began four months ago with diarrhea and vomiting. No acute pain in abdomen, but suffers with insomnia, cramps in legs, etc. Is emaciated and anemic. Skin harsh and dry; temperature normal. Abdomen tympanitic, tender on pressure. No tumor to be found. Vomiting continued, and patient collapsed and died August 17, 1891.

*Autopsy. Anatomical Diagnosis.* Multiple sarcomata of small intestine, with secondary nodule in liver; no other metastases; chronic nephritis; lymphomatous variety; fatty degeneration of heart muscle and liver; beginning pneumonia (right lung); general anemia and cachexia.

*Body* much emaciated and cachectic looking. Peritoneal cavity dry and free from adhesions.

Thoracic organs normal, except for beginning pneumonia in lower lobe of right lung.

*Spleen* measures 10.5 x 5.5 x 3.5 cm.; weighs 100 grams. Consistence firm; color, dark red.

*Kidneys* weigh together 510 grams; measure 14 x 7 x 4.5 cm. The capsule strips off readily, leaving a smooth surface mottled with gray, and light-red areas. The cortex is swollen, 10 to 12 mm. in thickness; the striæ very coarse, with pale, grayish-white patches and streaks. There are some healing infarctions in the cortex.

*Adrenals* normal.

*Liver* measures 27 x 18 x 7.5 cm., and weighs 1580 grams. In general it appears normal and is reddish brown in color. In the substance of the right lobe is a spherical area 2.5 cm. in diameter, of mottled, light, brownish-red, and gray color, surrounded by a zone of hyperemia. Its consistency is about that of the liver.

*Intestine.* At a point 265 cm. above the ileocecal valve there is a slight constriction produced by a new-growth in the mesenteric side of the intestine. This measures 2 cm. by 3.5 cm., occupying in its transverse direction with more than one-half the circumference of the gut. The growth projects only a little into the lumen; its central part is superficially ulcerated, the edges projecting and rounded. The superficial part is discolored and bluish; the deeper part is gray. It is dense and fibrous in appearance, and extends a short way into the mesentery; 27 cm. higher is another similar growth, with central ulceration and ele-



vated, rounded margins. 130 cm. higher is a third similar growth, projecting into the lumen, with central ulceration. There is, a short way above this, still another non-ulcerated patch of a smaller size, surrounded by a few submucous nodules of small size.

All the lymph glands, mesenteric, retroperitoneal, periportal, cervical, inguinal, axillary, etc., are normal, and there are no metastases from the tumor, except the one in the liver visible to the naked eye.

*Microscopic Examination. Intestine.* Section passing through a nodule in the intestine shows that the mucosa is necrotic, but its lower part is infiltrated with tumor cells. The submucosa is spread wide by tumor infiltration, and the same is true of the muscularis. The mesentery is everywhere densely infiltrated with the same cells. The tumor gives the impression of being not quite so uniform in character as in other cases, nor are the rounded cells so loosely arranged. The stroma is rather more abundant than usual and the tumor cells seem to lie each in its separate mesh. They are rather large, measuring 5 to 12  $\mu$ , the smaller ones having more deeply stained nuclei than the larger.

The nuclei are round and vesicular, with definite nucleolus and chromatin network. The protoplasm is pale and rather ragged.

*Liver* shows a dense infiltration with the tumor tissue, which separates and destroys the live tissue. In other places there are foci of tumor growth of irregular form and extent. These apparently blot out the liver tissue completely, with the exception of the bile ducts and connective tissue, although there are often islands of liver tissue isolated in such masses. The destruction of liver tissue is much greater than that of the kidney, where the tumor merely separates the elements.

The kidney is infiltrated with same tissue, so that the tubules and glomeruli are widely separated or isolated in the masses of the tumor. No actual pressure seems to be exerted upon these tubules, nor upon the glomeruli. Everywhere one gets the impression that there is a certain coherence about the tumor tissue, so that about a glomerulus it forms a radiating mass with definite radiating stroma.

CASE IV.—Hestor B., aged sixty years; black. (Medical No. 10180. Autopsy No. 1402.) August 14, 1899. Brought in a stuporous condition from dispensary, so that no history was obtainable. Marked dyspnea. Respiration shallow, with expiratory grunt. Breath sounds faint, but clear.

*Anatomical Diagnosis.* Tumor of mediastinum and heart; involvement of bronchial glands; acute and subacute pericarditis, with adhesions; cardiac hypertrophy and dilatation; thrombus in right auricular appendage; infarction of spleen and kidneys; cholelithiasis, with impaction of stones in common and hepatic ducts, etc.; arteriosclerosis; chronic diffuse nephritis (pale kidneys); diverticulum of esophagus; diverticulum of ileum, and colon.

*Body* of an extremely stout colored woman 161 cm. in length. The peritoneal cavity shows some adhesions. The pericardium obliterated by adhesions.



*Thorax.* Pleural cavity contains no excess of fluid, but on diaphragm on left side are a few elevated, granular patches. Pericardial layers densely adherent all over heart and are in most places bound to adjacent tissues. Over right side are numerous opaque, yellowish-white nodular elevations, which reach a diameter of 3 mm., and over right ventricle become confluent, forming a large patch. At base of heart in front of the root of the aorta is an elastic mass 8 x 6 cm., over which the left vagus nerve seems to pass. A similar mass, 6.5 x 5 cm., lies about the trachea behind the arch of the aorta, but does not compress the trachea. All of the pericardial lymph glands are enlarged, and on section show distinct nodules of a pearly white appearance. The two masses above described lie in the mediastinal tissues and are not within the pericardium.

*Heart.* On opening the right auricle is found to be rather small; foramen ovali widely open, 1 cm. about in diameter. Right auricular appendage contains a ragged, mixed thrombus. From lower portion of appendix spring a number of soft polypoid masses, which hang down into the auriculoventricular orifice. A similar mass hangs from the opening of the coronary sinus. On cutting through the ventricular wall, the two pericardial layers are seen bound together by a fresh fibrinous exudate, apparently deeply colored with blood. The wall of the right ventricle is thickened in general, but anteriorly wall is enormously thickened by a large tumor mass, 4 x 7 cm. in diameter. This almost entirely replaces upper portion of ventricular wall. The wall of ventricle below the conus arteriosus is also distended by a tumor mass 1.5 cm. in diameter, which apparently lies outside of the muscle, under the thickened pericardium. This plate-like mass extends up to pulmonary ostium, where it becomes fused with the mass surrounding the pulmonary vessels. The tricuspid valve is itself delicate, although the posterior segment is somewhat shortened; it is overhung by the tumor masses described above. The endocardium of the conus just below the pulmonary valves presents a few polypoid elevations. The muscular trabeculae over the septum are very highly developed and the probe can be apparently passed through the septum into the left ventricle. On opening left ventricle it is found the probe did not penetrate into its cavity, but merely into a large space between the trabeculae. Mitral valves are delicate, but apparently competent, as are also the aortic. There is a very moderate sclerosis of the aorta. The wall of the left ventricle is surrounded beneath the pericardium almost everywhere by a certain thickness of the tumor mass. This mass reaches its greatest thickness, 4 cm., about aortic orifice. About mitral orifice it measures 2.5 cm. The large mass described in the anterior portion of mediastinum has an appearance on section like that of the tumor mass in the heart, except that on section the central portion is necrotic.

*Lungs.* Glands at hilum show involvement in the tumor. The pleural layers are in general smooth and glistening, except at the apices, where there are some old scars. Lungs in general normal.

Spleen, liver, pancreas, intestinal tract, kidneys, axillary, inguinal, and retroperitoneal lymph glands show no especial changes.

*Microscopic Notes. Tumor.* Is very uniform throughout in every position in which it is found. It is composed of a dense homogeneous tissue, made up practically of one kind of cell, and these cells are so connected with one another as to form a fairly coherent tissue. There are, however, many loose cells among them. In the tissue which invades the heart and very frequently in the mediastinal mass, there are round spaces which resemble fat cells and which give the appearance of bone-marrow, infiltrated with the tumor. One cannot certainly see a cell body or laterally placed nucleus in these spaces. Bloodvessels are quite abundant through the tumor and are very thin walled, some of them contain, besides red corpuscles, numbers of lymphoid cells. Close examination of the tumor with the oil-immersion lens shows that the cells are more or less distinct and separate from one another. They have an extremely irregular cell body, which stains faintly pink, and the quite large vesicular nucleus, which is in many instances elongated so as to give the cell a somewhat fibroblast-like appearance. Most of them, however, are much more rounded. The nucleolus is not conspicuous, and in fact in most instances cannot be made out. These nuclei measure about 5 to 12 mikra, and the cell bodies are so irregular that it is difficult to measure them; they may be estimated, perhaps, at 8 to 14 mikra, averaging about 10 mikra. The great uniformity of these cells is very striking; they are supported by the most inconspicuous reticulum, which is hardly to be made out with the eosin stains, so closely do the cells lie together. There are occasional cells with rather more deeply stained nucleus, of smaller size and of more rounded form, which have the appearance of lymphoid cells, scattered among the others; in places these are fairly numerous. Mitotic figures are quite frequently seen in the tumor cells, which have then a much more deeply stained protoplasm than elsewhere. Another section shows the tumor to be composed of very coherent tissue, in which the individual cells can hardly be separated.

*Heart.* The heart wall is invaded by a tumor mass which isolates and apparently destroys many of the muscle fibers. The mass is fairly homogeneous and made up of cells which are quite closely packed together and form very dense tissue. The cells are not rounded and isolated as in other cases, but are elongated and twisted, sometimes forming bundles. Some of them show mitotic figures. The nuclei are very smooth, pale, and vesicular, and although in many cases they look round, this is apparently when they are cut across, and, perhaps, the majority of them are elongated. It is difficult to make out the protoplasm of the cells clearly, but in some instances it is ragged; in other cases quite smoothly outlined. The intercellular substance is not abundant. A nucleolus is not prominent in these cells. In places where the cells are furthest apart the protoplasm of the cells seems to ramify and come in contact with that of the next cell.



CASE V.—E. H. H. (Medical No. 13873. Autopsy No. 1842.) Died January 7, 1902. Personal history negative. Three months ago pain in abdomen, with a lump in the hypogastrium. No nausea or vomiting; no tenderness. Loss in weight and strength. Pain in abdomen has ceased recently; patient is emaciated. Abdomen prominent. Spleen not palpable. Large irregular tumor in lower abdomen covered by intestine, not moving with respiration. On rectal examination the mass is found to project from the anterior pelvic wall backward toward the sacrum. Blood count, 4,400,000; leukocytes, 13,500; hemoglobin, 65 per cent. Differential count, polymorphonuclears, 63 per cent.; small mononuclears, 13 per cent.; large mononuclears, 14.9 per cent.; myelocytes, 1.4 per cent. Urine negative.

*Anatomical Diagnosis.* Persistent thymus; lymphosarcomata of the intestine, with dilatation and ulceration of the ileum; metastases in the mesenteric, abdominal, and retroperitoneal glands, involving the pancreas and right adrenal glands; metastases in the liver, thymus, bone-marrow, and kidneys; cachexia.

*Body.* 170 cm. in length; somewhat emaciated; glands not especially enlarged. Axillary and inguinal glands are palpable.

*Peritoneal Cavity.* The serous surfaces are smooth and glistening. The omentum is much wasted and of a reddish color; it was attached over three large tumor masses above and to the right of the bladder. The lower mass on the right included the intestine just above the ileocecal valve. Loops of the ileum pass into the other masses, which are firmly adherent to the bladder and to the tissues about the rectum. The mesentery is much thickened throughout and full of small and large nodules. Near the cardiac orifice of the stomach, several large discrete glands the size of hen's eggs are found. Just below and behind the greater curvature of the stomach and median to the kidney is a hard, irregular mass the size of a cocoanut. On section this mass, which is adherent to the stomach and right adrenal, presented an irregular, mottled, grayish-yellow surface. Most of the growth is of an opaque, grayish color, but large, hard, yellow bands cut them up into irregular areas. In one end of the growth there is considerable softening and a small, irregular cavity, containing yellowish, purulent material. The tumor suggests a number of large glands massed together. The tail of the pancreas disappears in the tumor, and islands of grayish, opaque new-growth infiltrates some distance into the substance of the pancreas. The pancreatic tissue otherwise appeared softer than normal.

*Thorax.* A body measuring 11 x 4.5 cm. lies over the trachea, extending down as far as the right auricle, apparently a persistent thymus. On section the upper portion is pinkish gray in color and of an irregular, mottled appearance. The lower portion is homogeneous, grayish yellow, and opaque. Several large glands, 8 x 5 cm. in diameter, are found in anterior mediastinum. Also several large nodular masses, as big as walnuts, are noticed on the diaphragm. On section these nodules show a gray, opaque, almost homogeneous surface, broken by yellowish, firm areas. They are not encapsulated, but pass directly into the

muscle substance of the diaphragm. The pleural surfaces are smooth and glistening.

*Spleen* weighs 200 grams; is large. It is dark red in color. The Malpighian bodies are prominent as white pinhead points. The consistency is firm. No tumor nodules are evident. The capsule is smooth and without adhesions.

*Intestine.* The small intestine throughout, but especially in the lower part, shows grayish-white flat nodules, from pin-head size to large ones 6 to 8 mm. in diameter, situated in the mucous membrane. The other coats of the intestine were not involved. Peyer's patches somewhat swollen, occasionally showed similar small, gray nodules. 55 cm. from the pylorus the ileum disappeared into the first large tumor mass, which is the size of an infant's head. On opening the remainder of the ileum down to the ileocecal valve a wonderful picture is disclosed. The three tumor masses, before mentioned, consisted of dilated portions of the ileum, infiltrated with new-growth and continuous with tumor nodules in the mesentery. The walls of the intestines are much thickened; in some portions being over 3 cm. in thickness. On section they show a grayish-semitranslucent surface, crossed by yellowish and grayish strands of tissue. The mucous membrane is closely adherent over such areas, and the growth has also infiltrated the tissues surrounding the gut. The large nodules lying external to the ileum are evidently formed from coalesced mesenteric glands, which helped to form the large tumor mass about the intestine. On section such masses varied greatly in structure. Some portions were semifluid; others grayish yellow, homogeneous and opaque, and translucent mucoid areas are frequently seen. Large areas of hemorrhage and broken-down points of suppuration occur.

The dilated portions of the ileum varied in length from 8 to 12 cm., and included the portions of the bowel showing involvement of the intestinal wall. The most distended portion of the ileum measures 16 cm. transversely. The mucous membrane is ulcerated over these areas, having a mottled, grayish-red surface, covered in places with greenish-gray exudate. The third tumor mass extended to within 2 cm. of the ileocecal valve. The edge of the valve is somewhat infiltrated and small; irregular pendant nodules are found on its margin. The appendix and its mesentery are thickened and infiltrated with new-growth. The large intestine does not show any infiltration of its wall. The mucous membrane is injected and the solitary follicles everywhere enlarged. The appendices epiploicæ are thickened, and formed pendant nodular masses 6 to 8 cm. in length. On section these masses show the same appearance as the other tumor masses. Back of the rectum large masses of glands forming nodules as large as apples are found. These tumors had infiltrated into the surrounding tissue and bound the rectum and pelvic tissues into one solid mass. Their structure is similar to the other nodules described in the mesentery. The inguinal and iliac lymph glands are somewhat enlarged, reaching the size of an almond. They are freely movable, and on section show a more opaque surface than normal.



*Microscopic Notes. Blood.* The smear of the blood shows no excess of leukocytes.

*Bone-marrow* is composed of an almost uniform mass of cells, which are largely of one variety, and appear to be polygonal cells with large, vesicular nuclei. Among these cells are scattered a few eosinophile granules, but the majority have no granulation in the protoplasm. The protoplasm is rather ragged and rather scanty, but shows no specific granulation. The nucleus is sometimes doubled; it contains large, well rounded nucleolus. Mitotic figures are not infrequent. The cells measure 6 to 10 mikra, and average about 8. They form a very solid sort of tissue; among them there are moderate numbers of large, pale, phagocytic cells, of very irregular form, with very pale vesicular nucleus and vacuolated protoplasm. These frequently contain fragments of other cells. No distinct nucleated red cells can be seen. Some of the cells with eosin-methylene blue show curious blue staining in the marginal parts of the protoplasm. These are obviously the tumor cells, which occupy so much space in the bone-marrow, to the exclusion of the ordinary myelocytes. The eosinophile cells, when they are seen, are usually polymorphonuclear. There are a good many cells whose nuclei stain very black, and are very irregular in outline. Some of these are doubtless cells in mitosis, while others seem to be degenerating cells; in many of them the protoplasm contains dark granules. The tumor cells are frequently seen in the bloodvessels in the marrow. On the whole, the tissue does not look like marrow. There are practically none of the cells characteristic of that tissue, the whole structure being replaced by the foreign elements. The presence of cancellous bone, however, makes the situation clear.

*Tumor.* Section through one of the main tumor masses shows precisely the same appearance, even to the large, irregular, phagocytic cells which were observed in the bone-marrow, and which are quite conspicuous here, and the degeneration processes in the nuclei which made them stain so deeply. Many of these nuclei show beautiful mitotic figures. The measurements of the cells are the same as in the section of bone-marrow, averaging about 8 mm., while the phagocytic cells measure 20 mm. or more in diameter. Mallory's connective-tissue stain brings out only the most delicate and sparsely placed filaments of connective tissue, and great masses of cells seem to have no support whatever. The pelvic and retroperitoneal glands are largely replaced by the tumor mass, but their cells vary a good deal in size, some being as large as 15 mm.

*Thymus* is entirely replaced by the tumor and is recognizable only from remnants of Hassal's bodies, which occur here and there. The cells of the tumor are exactly as they are elsewhere, reaching a diameter of 10 to 12 mm. The supporting reticulum is in very small amount, and phagocytic cells are scarcely to be found, except in one section, which shows a great separation of the cells, and there they are quite numerous.

*Omentum* is infiltrated with the tumor, which here shows some very large cells, measuring 12 to 15 mm. These have very definite cell outlines, with clear protoplasms and rather irregular nucleus.

*Kidney.* There is at one point an area in which the tumor has infiltrated between the tubules, isolating them from one another. Its cells have the characters seen elsewhere.

*Spleen.* There are no areas of tumor growth, and the Malpighian bodies are normal.

*Pancreas* is densely infiltrated with tumor cells, so that the parenchyma is spread apart and the individual acini appear atrophic.

*Adrenal* is surrounded by a homogeneous tumor mass in which the large, pale, phagocytic cells are abundantly scattered among the tumor cells. This mass infiltrates into the substance of the adrenal separating the cells and extending to the medulla.

*Liver* presents a nodule composed of the same cells, which, however, make use of the live framework as their support, gradually obliterating the cells, which are, however, still visible far out into the tumor nodule. At the margin the tumor cells can be seen filling up the capillaries between the liver cells. In other places there are small foci of tumor cells apparently quite separate from any large mass.

*Intestinal* wall is thickly infiltrated with the tumor, which extends from the mucosa, where it separates widely the epithelial structures down into the submucosa and through the musculature to the serous surface. The submucosa is especially thickened.

*Stomach* appears not to be involved.

*Heart.* On the surface of the heart, besides one of the coronary vessels, there is a minute mass of the tumor in which the cells fixed in Flemming's fluid are seen to possess a smooth, rounded outline. Here, too, they measure 8 to 12 mm.

*Tonsil* is infiltrated throughout with the tumor tissue.

CASE VI.—Henry J., aged seven years; white; admitted March 28, 1903. Complains of shortness of breath, cough, weakness, and pain in chest. Family history and personal history unimportant.

Present illness began suddenly on February 15, when patient awoke with choking sensation and difficulty of breathing. This condition has gradually grown worse, and patient has become very weak. Has vomited occasionally and has had excessive night-sweats. No hemoptysis or hematemesis.

Coughs and expectorates some white sputum in the morning.

*Physical Examination.* Well-nourished boy, of good color; veins of neck full; glands of neck and axilla enlarged.

Chest full, almost barrel-shaped; symmetrical. Over right front, between sternum and nipple, in third and fourth interspaces, is a rounded, smooth prominence, containing a small ovoid, freely movable mass. Dulness on percussion over whole right front and back, but resonance is more marked over lower portions. Tubular breathing over right, upper lobe.

Heart sounds remarkably loud and clear.



Veins of abdomen engorged. Spleen felt—marked leukocytosis (lymphocytes predominating).

Percussion over left front of thorax is almost flat from sternoclavicular articulation to the sixth rib in midaxillary line. Cardiac dulness cannot be differentiated. To right of sternum the note is slightly resonant above the third rib.

Loud, prolonged tubular respiration heard in second and third left interspaces. The dulness is continuous with that of the liver and extends 7 to 8 cm. below the costal margin. Spleen extends 5 cm. below costal margin. Leukocytes, 230,500.

*Anatomical Diagnosis.* (Autopsy 2111.) Lymphosarcoma from the thymus or lymph glands, filling chest; invasion of pectoral muscles, of parietal pericardium and parietal pleuræ; beginning growth along root of lungs; enlargement of all lymph glands in body; large spleen; red bone-marrow of femur; emaciation.

*Body.* Body of an emaciated boy; rigor mortis present. No postmortem discoloration. Pupils equal. Cervical, axillary, and inguinal glands are large and firm, and can be plainly seen beneath the skin. The chest is prominent, protruding most markedly at the costal angle. Subcutaneous fat slight in amount. Peritoneal cavity contains about a quart of embalming fluid, containing formalin. The peritoneum is apparently normal. The mesenteric glands everywhere enlarged and rather firm. Diaphragm, sixth rib on the right side; sixth space on the left side. On separating the pectoral muscles from the ribs a soft, grayish, opaque tissue is found infiltrating the pectoral muscles and springing out through the intercostal muscles. Tumor, length, 18 cm.; in depth,  $9\frac{1}{2}$ ; in width, 15. The sternum is closely bound to the mass beneath. This mass extends from the clavicles above to project at and fill the costal angle. Laterally, the mass almost completely fills the left pleural cavity, being adherent, however, only over the sternum and cartilages; to the right, the mass projects almost as far, but does not fill the pleural cavity quite so completely. The tumor is densely adherent to the sternum and diaphragm, and to all the structures that rest upon the bodies of the vertebræ. Thick layers of the tumor grow from the hilum of the lungs out into the parietal pleura, forming blanket-like layers over the posterior half of the parietal pleura. This growth is thicker along the ribs, and finger-like elongations extend along the lines of the ribs 6 to 8 cm. beyond the line where the general layer ends. This growth also extends a short distance along the hilum of the lungs. The tumor is in the form of a large, irregular central mass, with lobes from the size of a large orange to small lobules of 1 to 2 cm. in diameter, projecting from the main mass laterally up and down. The surface of the mass is smooth, of a pale, opaque, gray color, with a few small, dirty, hemorrhagic reddish areas here and there. The consistence is very soft, and when squeezed the tissue breaks up like gelatin or agar. The cut surface presents a raised, soft, uneven appearance, with very little connective tissue, showing areas of degeneration, with

hemorrhage. A grayish, milky juice exudes in moderate abundance from the cut surface. Between the posterior wall of the manubrium and the adherent tumor is found what appears to be a large hemolymph gland. The esophagus, trachea, and aorta, with the vessels arising from the aortic arch, are embedded in the tumor mass. It is not difficult to dissect the tumor from the structures mentioned. No sign is evident of a thymus gland. The heart is completely enclosed in the tumor mass, which is in intimate and inseparable connection with the parietal pericardium; apparently everything but the endothelial lining of the parietal pericardium has been invaded and replaced by the tumor.

*Heart* appears perfectly clear from an external examination.

*Left lung* completely atelectatic, lies behind the tumor; otherwise normal.

*Right lung* much compressed; internal margin contains fair amount of air.

*Spleen* 16x11x4 cm.; weighs 400 grams. Surface smooth. Consistency soft; color, dark red; on section, of a deep reddish-brown color. Pulp very prominent; rather soft; trabeculae and Malpighian bodies inconspicuous.

*Liver*, 20x14x8 cm.; much changed by embalming fluid in the external half inch. On section, is of a red-brown color, apparently normal. No nodules found.

*Kidneys, bladder, rectum, stomach, and intestine* appear normal.

*Pancreas* and adrenal seem clear.

*Retroperitoneal glands*, especially at the hilum of the liver, are very large, grayish, and medullary in appearance. The glands in the region of the pelvis and the inguinal glands show the same appearance in all cases; the glands are definitely encapsulated, and are not matted together. On section through a rib, the marrow is certainly not increased in amount, and is of a reddish color. The marrow of the femur is rather soft and jelly-like; homogeneous and bright in appearance.

*Microscopic Notes. Tumor.* Section through the tumor shows widely scattered bloodvessels in a very sparse reticulum of extremely delicate fibers, and a mass of small cells of pretty uniform size, measuring 4 to 7 mikra. The cells are very uniform, rounded, with relatively large rounded vesicular nucleus, occasionally showing slight indentation. The nucleolus is fairly distinct. The protoplasm is scant and tends to be ragged in outline. The cells lie quite separate from one another, without apparent support. There are a few connective-tissue cells associated with the reticulum, but there are apparently none of the large phagocytic cells described in other cases. Section taken from the mediastinal mass is quite homogeneous throughout, and shows no areas of necrosis. Another section shows an infiltration of the tumor mass into the voluntary muscle, apparently in the pleural wall.

*Bone-marrow* is composed of a practically solid mass of cells, among which megalokaryocytes can be seen. Of the remaining cells, the majority have solid, deep green staining nucleus; some of these are distinctly normoblasts, while others show no hemoglobin in their protoplasm. Many have nuclei which are



indefinitely vesicular. They resemble lymphocytes and are present in great numbers. The other cells which occur in great numbers are the myelocytes, which measure 6 to 10 mikra, and appear distinctly larger than the tumor cells. There are relatively few very large eosinophile myelocytes. The abundant small cells with dense green staining nucleus measure only about 4 mikra, sometimes less. These have a sharp outline and an almost invisible protoplasm, there being only a rim of reddish granules about the margin. On the whole, the bone-marrow does not give the impression of having taken part in the tumor formation.

*Lymph gland*, invaded by the tumor, has lost its architecture completely. The cells which make up its tissue are practically like those described in the mediastinal tumor, and of the same measurements. There are, however, other cells present, which evidently came from the lymph gland. The architecture of the lymph gland is not absolutely obliterated, and one can recognize in a general way the outline of the sinuses.

*Liver* in general is normal. The capillaries are filled with cells of the type of the tumor cells, and the periportal tissues are everywhere infiltrated with similar cells. This suggests that possibly the condition was allied to leukemia or leukosarcoma. The cells in the capillaries of the liver are fairly uniform in character, but vary somewhat in size.

*Spleen* shows a great increase in the amount of the splenic pulp, which seems to depend chiefly upon increase in the blood content, and in infiltration with mononuclear cells of the type seen in the tumor. Most of these cells lie between the venules, but there are also many within them.

CASE VII.—E. D. W., aged fifty-seven years, admitted February 28, 1905; died March 22, 1905. (Medical No. 18146. Autopsy No. 2496). Personal history negative. Has had night-sweats; recently no appetite. Great prostration; lost ten pounds. Physical examination practically negative. No definite mass felt in the abdomen. The liver and spleen not enlarged. Red corpuscles, 3,820,000; leukocytes, 8600. Differential counts; polymorphonuclears, 78 per cent.; small mononuclears, 66 per cent.; large mononuclears, 2 per cent.; eosinophiles, 18 per cent.; mast cells, 1 per cent. Patient had large intestinal hemorrhage; died from its effects.

*Anatomical Diagnosis.* Multiple lymphosarcoma of intestine; nodules in the pancreas and left adrenal; adhesive pericarditis; chronic pleural adhesions; hemorrhage in the intestine (amebæ found in the intestinal contents during life).

*Body* is that of a slenderly built man, 178 cm. in length. Body is still warm. Rigor mortis not set in.

*Abdomen.* The peritoneal cavity contains no excess of fluid; surfaces are dry and glistening.

The abdominal organs are normally disposed. The stomach extends, perhaps, 15 cm. below the ensiform cartilage. The liver is also prominent below the costal margin. The spleen feels much enlarged and a firm mass is to be felt

behind it. The intestines show here and there areas of thickening, opposite which the mesenteric lymph glands are enlarged and pale. The colon is apparently distended in places with a dark blood-like fluid.

*Heart* shows nothing abnormal.

*Spleen* is enlarged; measures 13 x 9 x 6 cm. It is soft and flabby. On section, the Malpighian bodies are readily visible, and are of normal appearance, perhaps slightly enlarged. The splenic pulp is grayish, dark red in color, and somewhat swollen.

*Liver and kidneys* show no abnormalities.

*Stomach, pancreas, adrenals, and kidneys* were removed together. The stomach is found to be normal in general appearance. The mucosa has everywhere the normal appearance. It is everywhere easily movable. At one point, however, near the cardiac orifice of the stomach, the outer wall is densely bound to the pancreas. The pylorus is normal. The duodenum below the pylorus shows a good deal of thickening of the mucosa at a point about 6 cm. from the pylorus, so that two or three large folds stand up prominently and cannot be easily turned from side to side. On section, the pancreas is found to lie directly under these folds, which are greatly thickened, and thus quite sharply marked off from the surrounding tissue. The thickening seems to affect chiefly the mucosa and the submucosa, although the muscular layer is somewhat infiltrated. In the neighborhood of this area, at practically the same level, there is a diffuse thickening of the mucosa, throughout which some ulceration has occurred. Behind these areas we come to the head of the pancreas, with numerous adjacent nodules, which are found to have the appearance of lymph glands, but which on section show perfectly homogeneous, pearly white color. Bile can be squeezed through the gall ducts. In the neighborhood of the bile papillæ the intestinal folds are thickened and rigid. Just below this they have their normal soft appearance. The pancreas at its head end is fairly normal. In its middle portion it is normal to appearance. In its neighborhood there are a number of modified glands in which the pearly gray masses sometimes involve the whole gland and sometimes only a part are to be found. Toward the tail end of the pancreas the lobules of the pancreas become enlarged and pearly white in appearance, and quite widely separated. They appear to be in places practically converted into a tumor mass, apparently infiltrated, without the loss of their architecture by the tumor mass, and thus a much enlarged pancreas tissue is found to enclose the veins and ducts in their normal relation. Beyond the end of the pancreas there is a mass which is apparently composed of an almost solid tumor nodule, although it may consist of the much lighter pancreas tissue. At its central point is an area of necrosis throughout which the tissue is soft, opaque, and white.

*Adrenals.* The left adrenal is surrounded by the tumor and embedded in it. The outline of the adrenal can be distinguished, but is greatly swollen at one end and apparently infiltrated with the tumor. Surrounding this end, and like a cap,



there is a mass of tumor tissue which is grayish white in color. The upper portion of the adrenal is surrounded by and embedded in the tumor tissue, so that its own structure becomes very much spread out. The right adrenal is large and swollen looking, but does not appear to contain any of the tumor tissue.

*Retroperitoneal glands* are little, if at all, enlarged.

*Intestines* were filled up to a high point in the ileum with fresh, bright blood, part of which was clotted in cylindrical clots, was firm, and was apparently affected by the contraction of the intestine. The mucosa of the colon is much stained by the blood. At one point in the upper portion there is a small rounded area which has somewhat the appearance of an ulceration, from the centre of which there projects a little mass of the mucosa. This measures 1, 2, or 3 mm. in diameter. The lymphoid nodules are not especially prominent. There are no definite ulcerations in the colon. The appendix is normal looking for its first third. No lumen can be found past that. Above the ileocecal valve the folds of the mucosa are normal in appearance. Peyer's patches are normal until a point is reached about 30 cm. from the ileocecal valve, where the folds become very much thickened, very rigid and very firm, and the whole intestinal wall is thickened. The central portion of this area, which stretches around the circumference of the intestine, that is, the portion apparently opposite the mesenteric attachment, is quite deeply ulcerated, ragged, and necrotic on the surface. The outer surface of the intestine at this point is paler in color than the neighboring intestine, and may be easily recognized by its induration. Over it there run numerous tortuous, perhaps distended, bloodvessels. The lymphatic vessels are also distended. The adjacent mesentery contains an enlarged lymph gland, which, on section, is perfectly homogeneous and pearly-white in color. From this point on the intestinal folds are again normal for about 40 cm., where there are to be observed minute patches of thickening in the course of some of the transverse folds. These form merely little nodules and are quite free from any ulceration. A few centimeters past this there occur large areas, measuring perhaps 3 cm. in length; two such areas being separated by a gap of about 2 cm., and completely encircling the intestine. These have precisely the character seen in the first areas described, that is, they produce a great thickening and rigidity of the folds of the intestinal mucosa and also an infiltration of the submucosa and muscularis. There is a central ulceration from which probably much of the blood originated. Over the serous surfaces the lymphatics can be quite plainly seen running from this area toward the mesentery; 15 cm. higher there is another encircling patch, in which the thickening of the mucosa is not very striking, and there is no ulceration. From there on the mucosa is normal, although covered with blackened blood for about 50 cm., where there is another patch of thickening of slight degree extending for about 4 cm. Probably the other minute patches escaped attention, being hidden by the thick, sticky, black material, which can hardly be removed without completely destroying the mucosa. From this point on, the intestine is normal for about 50 cm, when there

are small scattered thickenings of the folds, involving only one or two folds at a time throughout part of their transverse course. This is repeated at an interval of a few centimeters, after which the intestine is normal for 50 cm. or more. Then there appears again a quite similar patch. Above that the intestine is normal; folds are quite soft and pliable. From here for a distance of perhaps 100 cm., up to the upper end of the ileum, there are practically no more thickenings until we reach a point about 100 cm. from the place where the duodenum was cut through, and there is a patch involving six folds completely encircling the intestine and causing great thickening and rigidity of the folds. This thickening here involves noticeably the mucosa, the submucosa, the muscularis, and the subserous tissue. There is no ulceration on the surface of these thickened folds. Another such patch, rather smaller in extent, occurs about 10 cm. above this. Such patches do not always encircle the intestine, and the next one above at a distance of about 10 cm. leaves a gap through which the mucosa is practically normal. Above this there are scattered thickenings of individual folds. The jejunum and the upper extremity of the ileum contain numerous such patches, separated by intervals of a few centimeters. The mesentery contains large glands which have the same pearly color throughout, as described in the intestinal thickenings.

*Microscopic Notes.* The tumor tissue wherever it occurs is composed of a very delicate reticulum, in the meshes of which the cells lie quite loose. They are uniform in size and general appearance, with rounded, slightly ragged outline, and somewhat granular protoplasm.

Smears stained with Ehrlich's triple stain show, however, no specific granulations in their protoplasm. The nuclei are large and vesicular, with definite, deeply stained nucleolus. The cells measure 8 to 12 mm. in diameter.

*Intestine.* The intestinal mucosa is infiltrated with the tumor cells. The villi, although still thinly covered with epithelium, are distended into a bulbous form by great numbers of the tumor cells, which are here, too, remarkably uniform in character; mitoses are abundant among them. In the superficial layers there are many wandering cells in the ulcerated places, and these are polymorphonuclear leukocytes; infiltration extends through the muscle and through the subserous coat.

*Bone-marrow* is very cellular. The fat cells are widely separated by masses of other cells, which are chiefly mononuclear. These cells resemble almost precisely the cells of the tumor and have the same morphology. Their protoplasm is, perhaps, slightly more ragged than that seen in the tumor. They measure 8 to 12 mikra, and are thus just the same size as the tumor cells. A few mononuclear cells are eosinophiles, but the majority of the cells in the bone-marrow are of the type just described, showing no definite granulation in their protoplasm; of course, these may be neutrophile myelocytes. No smears were preserved from the bone-marrow, so that Ehrlich's stain cannot be applied. There are very few evidences of new formation of red corpuscles. In the veins



of the bone-marrow there may be seen at times numbers of large, dense, red-staining cells, with vesicular nucleus. In another section, stained by Borrel's method, the cells stand out prominently with beautiful vesicular nucleus, with ragged, greenish protoplasm. They are almost the only cells discernible.

*Pancreas* is extremely, densely infiltrated with cells, so that the acini are widely separated, and the gland could scarcely be recognized. The islands of Langerhans are similarly invaded, but they hold together better than the rest. The infiltrating cells are practically of one character, as is described above, and have the same measurement.

*Mesenteric lymph gland* still shows its architecture, but the lymph cords are almost entirely replaced by tumor cells, lymphoid cells being present in relatively small numbers and recognizable by the smaller size of their nucleus, and their less abundant protoplasm. In the sinuses there are many of the tumor cells, and there are also numerous large polygonal cells of phagocytic character, with pink-staining protoplasm, which are easily distinguished from the tumor cells. The tissue around the mesenteric glands is also quite densely infiltrated with the same tumor cells, and numerous larger cells of polyblastic character. In the mesentery the lymphatics, which are recognizable by their peculiar valves, are found to contain masses of cells, largely polymorphonuclear leukocytes and large phagocytic polyblasts, but there are also many cells resembling the tumor cells.

*Testicle.* Section of the testicle shows one area where the tubules are separated widely by the mass of a tumor which has the same composition as before, although the cells are, perhaps, a little more elongated.

*Adrenal* is completely infiltrated with the tumor, which isolates the elements of that tissue from one another, so that each two strands of the cortical cells are separated by infiltrating tissue. This extends also into the medulla and forms a mass outside of the adrenal.

*Spleen* shows no tumor nodules nor are there any scattered cells which can be recognized as tumor cells, although there are some cells in the capillaries which might possibly represent them.

CASE VIII.—R. S. S., aged seven years; white. (Medical No. 18008; autopsy No. 2543.)

*Personal history* negative. Six months before death noticed swelling of cervical glands. Nodules were felt in the abdomen at the beginning of the affection. Patient vomited a good deal and lost in weight. Examination January 23, five months before death, showed large prominent masses on both sides of the neck, the larger being firmly fixed. The axillary and inguinal glands readily felt. Red blood corpuscles, 3,344,000; leukocytes, 9800. The tonsils are greatly enlarged, firm and elastic; no ulceration. The abdomen is distended, filled by a large irregular mass of firm nodules, which seem not to be attached to the abdominal wall, some of them as large as an orange. Spleen is not palpable. Differential count: polymorphonuclears, 79 per cent.; small mononuclears,

10 per cent.; large mononuclears, 8 per cent.; eosinophiles, 1 per cent.; transitional form, 2 per cent. A gland removed for diagnosis, January, 1905, shows considerable areas without any tumor, which look normal. The sinuses contain blood. Other areas are entirely distorted by the presence of tumor masses. In the least involved parts there are round, sharply circumscribed areas in the centre of the lymph cords, which are identical in structure with the larger masses. These are composed of larger cells than the lymphoid cells, with vesicular nucleus and a nucleolus. The nuclei are much paler than those of the lymphocytes, and show frequent mitoses.

*Anatomical Diagnosis.* Lymphosarcoma, involving intestines, pancreas, adrenals, spleen, lymph glands, and stomach.

The glands excised from the neck several months ago show the presence of a metastatic round-cell growth. The structure of the glands was not destroyed but there were circumscribed areas of tissue composed of large round cells, lying in a delicate stroma. Only the abdominal organs were sent, not including the liver. The stomach is not enlarged. From its anterior edge there hang large, rounded masses of soft consistence, composed of a fairly homogeneous, pearly gray tissue. The mesenteric glands are separately enlarged into round nodules. The intestine is everywhere almost sessile on this mass of enlarged mesenteric glands. The spleen is not enlarged; measures 8 x 5 x 3 cm.; is fairly firm in consistence. The trabeculae and Malpighian bodies are readily visible. There are some larger grayish nodules scattered through its substances which resemble tumor masses. They are gray and translucent. The kidneys show no special abnormality.

*Adrenals.* The left is bound up in a tumor mass, but is apparently normal. The right is invaded by the tumor, the medullary portion being pale pearly gray, while the cortical portion lies as a yellow band quite sharply marked out between this and the surrounding mass of similar pearly gray soft tissue. The contours of the organ are well preserved. The aorta and vena cava are deeply embedded in a mass of enlarged lymph glands, which are soft and pasty, and on section are pinkish gray, with small areas of opacity. They reach a diameter of 4 cm. in places. The colon is closely bound to the stomach by the intermediation of nodules and adhesions. The rectum is apparently normal. As one passes up the large intestine, one finds scattered areas of thickening, which are firm, and over which the mucosa is well preserved. These may involve transverse folds, which stand out rigidly. In the cecum nearly all the folds have this character. The ileocecal valve is thickened into a stout ring. Peyer's patches above the ileocecal valve are greatly enlarged and form stout, projecting masses. On passing up through the ileum, numerous patches are found, throughout which the transverse folds are rigid and elevated. These are extremely numerous, especially up toward the upper end of the ileum, where they sometimes form great thickenings. There is hardly any ulceration at any point. The duodenum is particularly affected by the great thickening of the



Quite the same type of tissue is found to invade the cortex and medulla of the mucosa. Its folds are enormously increased in bulk, and are swollen so as to touch one another at their crests. The mesenteric glands on section have the same appearance as the other enlarged glands. They show extensive areas of softening and some yellow, opaque, necrotic patches.

*Pancreas* is practically replaced by the tumor. Its lobulation is still apparent, but is almost completely masked by the extreme infiltration with the tumor.

*Spleen.* The Malpighian bodies are normal in appearance. There are several quite sharply circumscribed areas of tumor tissue compressing the adjacent splenic pulp, and pushing aside the trabeculae. These are often in very close contact with Malpighian bodies, where it can be seen that their cells differ markedly from those of the Malpighian bodies, partly in being almost twice as large, and partly in the fact that the lymphoid cells of the Malpighian body have a rather darker stained nucleus, and a very much more sharply outlined cell body. They measure 5 to 8 mikra, while the tumor cells measure 8 to 12 mikra.

The cells of the tumor are fairly uniform and round, and lie quite loose in a very scanty supporting reticulum. The protoplasmic outline is somewhat ragged; the nucleus large, round, and vesicular, with a very distinct nucleolus and deeply stained chromatin particles around its margin. In some of the cells the protoplasm is denser and takes a deeper red stain, and then the nucleus appears shrunken. Mitotic figures are especially abundant in these cells, and it seems probable that the deeper stain of the protoplasm is associated with this process of division. There are some small lymphoid cells with deeply stained nucleus scattered among the tumor cells, but these, since they do not occur in tumor nodules in the other organs, are regarded as wandering lymphocytes. There are occasionally seen very large cells with indefinite outline and extremely pale vesicular nucleus. These are actively phagocytic and are frequently seen to contain remnants of other cells.

*Duodenum.* The mucosa is infiltrated thickly with cells such as were described in the spleen. Here they occur unmixed with other cells, and are uniform in type. There are none of the wandering lymphocytes seen in the spleen, but there are a few of the large, pale, phagocytic cells. Occasionally cells, otherwise like the tumor cells, but very large and with several nuclei, are found.

The underlying Brunner's glands are infiltrated with the same tissue, and remnants of the glands of the mucosa are to be found embedded deeply in the tumor tissue, but the villi are denuded of epithelium, and are enormously thickened by the infiltration. The musculature, too, and the subserous tissue are densely infiltrated.

*Mesenteric glands* show that their structure is obliterated, and they now consist of masses of rounded cells lying in a delicate reticulum. The surrounding tissues and the subcapsular layer of the gland are infiltrated with lymphoid cells. Mitoses are abundant among the tumor cells, and the large phagocytic cells occur in numbers.

adrenal, which is almost entirely replaced by the tumor, here, again, in a very pure condition. The cortex is much less involved than the medulla, although in places it, too, shows extensive infiltration; outside there is a thick mass of the tumor.

*Pancreas* has suffered in the same way and is converted into a solid mass of the tumor, with scattered pancreatic elements.

The mucosa of the stomach is densely infiltrated with the same cells somewhat mixed with other cells of the type usually seen in the mucosa.

From this record of cases it is seen on analysis that of the 8, 3 cases were essentially intrathoracic tumor growths (Cases I, IV, and VI), while in 5 cases the abdominal organs were chiefly involved, the most striking and the only constant lesion being that of the digestive tract. Thus it seems possible to divide these cases fairly sharply into two groups, of which the first is composed of cases, in which there is a tumor growth in the mediastinal tissues, while the second comprises those in which there are single or multiple tumor growths in the intestinal wall, extending or metastasizing thence to other abdominal organs, occasionally to more distant structures.

The 3 cases which show a mediastinal tumor growth extended to the other thoracic tissues as follows: Pericardium, 2 cases; myocardium, 1 case; pleura, 2 cases; bronchial glands, 2 cases; pectoral muscles, 1 case; cervical lymph glands, 2 cases; other lymph glands, 1 case; tonsil, 1 case. In no instance was there any metastasis to the spleen, liver, or other abdominal organs. This in itself seems to confirm strongly Kundrat's idea of the regional distribution of these tumors, and shows, perhaps, that they are not quickly spread about by the blood stream. It is curious that in one of these cases (Case IV) soft polypoid masses of the tumor actually hung in the cavity of the heart, and still there were no metastases which could be regarded as due to transportation of cells by the blood stream. The extension by lymphatic channels is, however, apparently easy, and not only do the bronchial and cervical glands become involved, but occasionally even more distant glands. The serous surfaces may be affected by the appearance of nodules or plates in their substance, but in one of our cases (Case III) the mediastinal mass was such that the pericardium was rendered quite rigid and the heart beat in a circumscribed cavity hollowed out of the tumor.



Histologically these thoracic tumors are seen to be somewhat different from the rest in that they are composed of rather smaller cells. Of course, one cannot generalize from so few cases, but in these 3 cases the cells measured 5 to 8 mikra, 5 to 12 mikra, and 4 to 7 mikra, respectively. There were in none of them the large phagocytic cells so common in the abdominal forms. It is true that Case IV was peculiar in showing a rather coherent tumor tissue, but otherwise it resembled the other 2 cases very closely.

It is surprising to find that a fairly well outlined picture is produced by the second group of cases, in which the intestinal lesions form the constant feature, and in which they appear to be the oldest lesions.

There are 5 cases (Cases II, III, V, VII, and VIII), and these showed, in addition to the intestinal growth, lesions elsewhere as follows: liver, 2 cases; stomach, 2 cases; pancreas, 2 cases; adrenals, 3 cases; kidneys, 2 cases; mesenteric glands, 4 cases; thymus, 1 case; bone-marrow, 1 case (possibly 2); tonsil, 1 case; testicle, 1 case. In 3 of the cases (Cases III, VII and VIII) the intestinal lesions formed many patches of thickening of the intestinal wall, which did not produce narrowing, but rather the reverse. In these cases ulceration was not very advanced, and in some of the patches it might be easily overlooked. In these places the thickness of the valvulæ conniventes, which stood up stiffly, much swollen by the infiltration of cells, was striking. Such prominent portions of the mucosa soon become ulcerated. In the other 2 cases the dilatation of the affected portion of the intestine was enormous, so that the gut appeared to open into a great cavity in a mass of the tumor. On careful examination the mode of involvement of the intestinal wall was seen to be similar to that in the other cases, although more extensive. In another case, seen at autopsy in Professor Weichselbaum's laboratory, in Vienna, the intestine throughout considerable lengths, was converted into a rigid, thick-walled tube. In that case the distribution of the metastases resembled that seen in this series.

In 2 cases there were single nodules in the liver, while in 3 cases both pancreas and adrenals were surrounded and densely infiltrated with the tumor substance. It seems probable that this affection of the pancreas and adrenals was due to extension of the

tumors from adjacent affected lymph glands, but we must suppose that the cells reached the liver by the blood stream. This is true too, in the 2 cases in which the kidneys were infiltrated, and in one with a similar affection of the testicle, and probably the involvement of the thymus in 1 case, must also be regarded as hematogenous. In 2 cases the mucosa of the stomach was thickened by the accumulation of cells in much the same way as the intestinal mucosa.

It is generally stated that the bone-marrow is not affected, but in 2 of these cases, of 3 in which the bone-marrow was examined it was found to be markedly altered and largely occupied by cells which closely resemble those of the tumor. In the remaining 3 cases from the group of intestinal tumors no bone-marrow was saved.

Histologically the members of this group agree very closely with one another. Their cells are rather larger than those of the thoracic tumors, measuring 6 to 14 mm.; 5 to 12 mm.; 6 to 10 mm.; 8 to 12 mm.; 8 to 12 mm.; or an average of 6.6 to 12 mm. There are also large phagocytic cells among the other cells in these cases, although they are not found in the 3 cases of thoracic tumors.

**DIAGNOSIS.** There is no difficulty in distinguishing the tissue from a case of lymphosarcoma from that in Hodgkin's disease. On the other hand, it is not easy to distinguish the altered tissue of the lymph glands, and other nodular areas in leukemia, from that in lymphosarcoma. There are, however, other aids to diagnosis than the mere examination of a section, for the blood shows the leukemic change.

Evidently the line to be drawn between leukemia and lymphosarcoma is not a very definite one, for cases are described in which a lymphosarcoma without leukemic changes in the blood subsequently developed them, and, indeed, as is stated above, in one of our cases (Case VI), there was a distinct, indeed a very great, increase in the number of lymphoid cells in the blood, with corresponding changes in the bone-marrow. Hence this case is probably wrongly included in the group of lymphosarcomata according to this morphological subdivision, and should probably be classed as a case of leukosarcoma. Its existence justifies in our mind Sternberg's setting up of that subdivision. Again, there are numerous cases of leukemia,



long recognized as such by the blood findings, in which there develop toward the end of life such enormous packets of enlarged glands, with masses of lymphoid tissue in the liver, spleen, and other organs, that it is difficult to resist the idea that here we have to do with an infiltrating process somewhat similar to that seen in the recorded cases of lymphosarcoma; even in the acute cases of leukemia such lymphomatous nodules, or areas of infiltration, may be found in the kidney and liver, which rouse doubts in one's mind as to the relations that should be recognized between the two conditions. Nevertheless the actual destructive processes which characterize the lymphosarcoma are absent here, the bone-marrow changes are prominent and the morphological distinction is made.

Cases illustrative of this may be recorded briefly here, although they are, of course, familiar to everyone.

Patrick O'C., aged sixty years; admitted March 25, 1896; died January 31, 1899. (Medical No. 5934; also 8408, 9292.) Complains of shortness of breath; has lost much weight. Six months ago noticed small swellings in the inguinal regions, which have steadily enlarged. Red corpuscles, 3,820,000; leukocytes, 241,140.

*Spleen* palpable. In the right axilla there is a bunch of glands 5 x 4 cm. The glands are separate. The inguinal glands form a large compact mass on each side, and there are large masses above Poupart's ligament. May 5, 1896. Hemoglobin, 50 per cent.; red blood corpuscles, 3,148,000; leukocytes, 675,000. Differential count: polymorphonuclears, 4.1 per cent.; large and transitional mononuclears, 0.6 per cent.; small mononuclears, 95 per cent.; eosinophiles, 0.2 per cent. Spleen extends 11 cm. below the costal margin, flatness above beginning at seventh rib.

Second admission, two years later on account of increased enlargement of the glands. Loss in weight and shortness of breath. Cervical glands not enlarged. Axillary glands greatly enlarged. Spleen not palpable. Masses in the groins very large, apparently composed of separate glands. The mass measures in the right groin 20 x 17 cm.; in the left, 8 x 13 cm.

*Anatomical Diagnosis.* (Autopsy No. 1261.) Blood picture of lymphatic leukemia; general lymphatic hyperplasia with tumor masses in inguinal and retroperitoneal adhesions; infiltration of hepatic vessels, spleen, pancreas, and lungs; splenic tumor; lymphoid bone-marrow.

Large tumor masses in inguinal regions over which skin is tense and cyanotic. The masses are continuous with others in the pelvis. The intestinal loops are displaced by large retroperitoneal tumor masses. The tumor masses on each side narrow the pelvis into a funnel-shaped opening. The omentum contains

several enlarged glands. The spleen measures 18 x 9 x 5.5 cm. The Malpighian bodies distinct. From the splenic substance there project two nodules, one measuring 1 x 1.5, and the other 0.5 x 0.05 cm., the smaller surrounded by a pigmented area. The liver not enlarged. No gross tumor nodules. Infiltrations of whitish material accompany the portal vessels running in the adventitia, but sometimes projecting into the intima, or even into the lumen of the vessel. In the larger vessels these may be developed on one side, while in the smaller it is often annular. Invasion of the liver tissue proper is not especially evident.

*Kidney, adrenal, thyroids, and testicles free.*

The inguinal tumors measure on the right side 40 x 31 x 33 cm.; on the left, 25 x 8 x 7 cm. They are nodular, the nodules being bound together more or less closely through the invasion of the gland capsules and periadenoid tissues. The skin over the tumors is also adherent. On section the glands are uniform or slightly variegated by congestion and ecchymoses. No extensive necroses are seen, but small foci of yellow may be made out. The masses developed from the pelvic and retroperitoneal glands are similar; they measure 26 x 28 x 8 cm. This mass is continuous with the peripancreatic glands where the tumor extends into the pancreas. Bronchial, tracheal, and cervical glands enlarged and bound together. The individual glands in the neck region are fairly well separated. The bronchial glands seem to invade the lung for a short distance. Axillary glands are uniformly enlarged. Bone-marrow firm and lymphoid in character. Stomach and intestines normal.

William W., aged sixty-four years; admitted December 25, 1899. (Medical No. 10721.) Gradual weakness began two years ago. Lumps in axilla and inguinal regions were noticed three months ago. At present posterior cervical glands slightly enlarged. Axillary and inguinal glands enlarged. Spleen is distinctly felt 5 cm. below the costal margin. Red corpuscles, 4,912,000; leukocytes, 133,400; differential count: polymorphonuclears, 19.6 per cent.; small mononuclears, 79.1 per cent.; eosinophiles, 0.7 per cent.; mastzellen, 0.6 per cent. Blood culture shows streptococci before death.

*Anatomical Diagnosis.* (Autopsy No. 1471.) Lymphatic leukemia; enlargement of all lymph nodes; lymphoid nodules throughout liver; chylous ascites.

Periportal and pelvic lymph glands are much enlarged. Bone-marrow purplish, translucent, and somewhat gelatinous. Femoral lymph glands measure 4 x 2 x 7 mm.; pale, homogeneous, and elastic on section. Aorta in front of the lumbar and dorsal vertebræ is surrounded by a matted mass of glands. The thoracic duct passes through, but is not compressed. The mesenteric glands show small, opaque, yellowish dots; one large mass in the neighborhood of the duodenum contains an anemic infarction about 1 cm. in diameter. The lymphoid tissue is increased throughout the intestine. Other organs are normal in appearance. The pancreas is almost entirely buried in the mass of enlarged glands which surround the duodenum. Spleen weighs 1320 grams; measures



24 x 15 x 9 cm. There are large wedge-shaped infarctions. The Malpighian bodies are irregular in outline, sharply defined, pulp grayish purple, with a few scattered hemorrhages. The consistency is diminished.

*Microscopic Sections.* The spleen shows abundant lymphoid cells in the venules and in the intercapillary tissue. The liver capillaries are also filled with them. The kidney shows numerous lymphoid masses in the cortex and about the vessels in the boundary zone. The left ureter is thickened by an infiltration with lymphoid cells. The bone-marrow is densely infiltrated with lymphoid cells, and shows relatively few eosinophiles and myelocytes. The lymph glands show a mass of lymphoid cells, the architecture no longer distinguished. Testes, intestine, and subserous tissues are infiltrated with lymphoid cells.

A subdivision of the cases of fairly typical lymphosarcoma into two groups has been made, but it is, of course, not to be claimed that all cases of lymphosarcoma will fall clearly into one or other of these groups. It is probably, to a certain extent, an accident that ours do so, for it is easy to see from a review of the rather confused literature that there are many cases in which different distribution of the lesions is recorded, and doubtless, as stated by Kundrat, any region of lymphoid tissue may be the starting point for such growths. The character of the growth and its mode of distribution is, however, distinctive enough, and so is its histological structure.

In contrast with this, a case may be recorded in which it is somewhat difficult to settle the diagnosis in this regard.

E. E. H. (Medical No. 18907.) Personal history negative, except for a previous admission, October, 1906, when the liver and spleen were enlarged and large lymph glands were found in the neck, axillary and inguinal region; thought at that time to be Hodgkin's disease. Tubercle bacilli found in the sputum. Fluid was aspirated from the right pleura. Present illness began two weeks ago, with edema of the legs. Red corpuscles, 2,678,000; leukocytes, 1980. Differential count shows practically normal relations.

*Spleen* greatly enlarged; extends 11 cm. below the costal margin. The legs edematous. Cervical, inguinal, and axillary glands palpable. Frequent aspiration of the right thorax, with removal of enormous quantities of fluid. Edema of abdomen and legs. Collateral circulation developed in subcutaneous veins of the abdomen. Total amount of fluid removed, 75,500 c.c., January 5. Differential count: Leukocytes, 5900; polymorphonuclears, 80 per cent.; eosinophiles, 4 per cent.; small mononuclears, 10.5 per cent.; large mononuclears, 2 per cent.; transitionals, 1 per cent.; myelocytes, 2 per cent.

Edward H. (Ward E.). Died 11.50 A.M., February 3, 1907. (Autopsy No. 2839.)

*Anatomical Diagnosis.* Sarcoma of lymph glands; involvement of retroperitoneal and pelvic glands; invasion of adjacent muscles and vertebræ; extension to pelvic peritoneum and pleura, and intercostal muscles, pericardium, etc.; nodules in lungs and bronchi, bronchial and mediastinal glands, cervical, and inguinal glands; chronic, splenic tumor; hyperplasia of bone-marrow.

*Body* is that of an emaciated white man, 184 cm. in length. Edema of the left leg. The peritoneal cavity contains a liter of fluid. The spleen is greatly enlarged; it extends 12 cm. below the costal margin. Some opaque, whitish patches project underneath the serous surface, especially in the pelvis. The right pleural cavity contains 2000 c.c. of turbid fluid. The left pleura is obliterated. In the anterior mediastinal tissue, and extending through the intercostal muscles between the third, fourth, and fifth ribs, is a mass of uniform pinkish-white tissue.

*Heart* is not abnormal.

*Left lung* is compressed, but in most places air-containing. It shows a few small, firm nodules, which resemble on section the new tissue seen in the anterior mediastinum. The bronchial glands are enlarged, and partly occupied by white masses of tissue of the same type. One branch of the bronchus running toward the apex shows at about 4 cm. from the apex a thickening of its wall for a distance of 1.5 cm.; the thickened wall is white and opaque, and evidently there is an infiltration of the new tissue to produce a wall 2 mm. in thickness; distal to this the bronchus is normal.

*Right lung* shows no such nodules, but throughout both lungs there are minute, tubercle-like nodules.

*Spleen* weighs 100 grams; measures 23 x 14 x 6 cm. It is large and tense, and dark purple in color. The notches anteriorly are very deep. The appearance is quite uniform throughout, but the consistency is not quite uniform. On section there are found nodules of foreign tissue, but the spleen is mottled with areas of deep red and areas of paler red. The Malpighian bodies show faintly, trabeculae and vessels are prominent, and the splenic pulp seems rather firm and swollen. The dark-red areas seem firmer than the paler parts.

*Liver, stomach, adrenals, kidneys, and intestines* show no abnormality.

*Aorta and vena cava inferior* are embedded in a firm nodular mass, but where they are opened there is found to be no absolute obstruction, even though the vessels be somewhat compressed. This is true also of the iliac vessels and, perhaps, especially of the left femoral vessels, which are followed by the nodular mass of Poupart's ligament.

All of the tissue in front of the sacrum and the muscular walls of the pelvis seem to be occupied by conglomerated tumor nodules. The masses are more or less discrete, but cannot be very easily separated. The same nodular mass extends about the aorta and behind it in the retroperitoneal tissue, along almost the whole of the vertebral column, being very tightly adherent to the vertebræ in the lumbar region, where they have to be carved off. The thoracic duct could



not be found, in spite of careful search. The tissue making up the nodules is everywhere of about the same appearance; it is uniform, firm, pale, pinkish white, with but little indication of a separate stroma. It is glistening, not translucent, moist, with no areas of especial opacity. Hemorrhages are very uncommon and bloodvessels are inconspicuous in the masses. The nodules appear to represent preëxisting glands, but the tissue does seem in many places to break through the capsule of the glands, so that the masses are bound very tightly together, so as to form a coherent mass. That the capsules of the glands do not form a definite limit is shown further by the fact that the ileopsoas muscles on both sides and, indeed, all the adjacent muscles are infiltrated with the same substance, which appears in the form of scattered nodules stretching far and wide through the pale muscle. Some of these seem to be quite isolated in the muscle substance. Similar invasive properties are shown in the intercostal muscles, and described. The vessels are nowhere invaded, and their intimal lining is everywhere smooth. There are no thromboses. A piece of this tissue was introduced subcutaneously into a rabbit February 4, which remained well. The glands are filled with the tissue about the arch of the aorta, and out along the subclavian arteries. Masses extend also into the neck, but do not pass the thyroid gland. On cutting into the lumbar vertebræ, where the tumor mass is especially adherent, the bone-marrow is found to be very deep red, but opaque, pinkish-white areas extend into it and apparently represent tumor extensions.

*Bone-marrow* of the femur is soft and very deep red. There is practically no fat left in it, but the accumulation of cells is not sufficient to give it a firm texture, and it is almost diffuent.

Smears from the tumor stained for spirochetæ negative.

Smears from the tumor stained for tubercle bacilli negative.

*Microscopic Notes.* *Bone-marrow* shows no cells resembling the tumor cells, very few polymorphonuclear leukocytes, many myelocytes, and megalokaryocytes. There are areas of lymphoid cells, almost unmixed with other cells. Tubercles are seen in the bone-marrow.

*Spleen, lungs, etc.,* show tubercles.

*Pleural* shows tumor nodules composed of the tissue to be described. The thickening of the bronchial wall is due to an infiltration with the tumor tissue. Some of the mucosa is still present over this thickened patch, and bits of cartilage and glands are embedded in it.

*Tumor.* The tumor itself is very uniform wherever it occurs. It invades lymphatic glands in the form of an expansive growth, and it is sharply outlined from the lymphoid tissue, which it pushes in front of it, not only by the paler stain, which its cells take but by their difference in size and general appearance. The connective-tissue stroma of the tumor is rather delicate, consisting of very fine meshwork of fibrils, attached to the bloodvessels, which are fairly abundant. The tumor is essentially composed of cells of one type. These are large and elongated, or round, or polyhedral in outline. The lymphoid cells measure 4 or 5 mikra, while the cells of the tumor average 9.9 mikras in diameter. The

nuclei average 6.3 mikras. The cells are sometimes irregular in outline, with processes which reach off to touch those of other cells. The protoplasm is finely granular. The nuclei are rounded and vesicular, with a fairly distinct nucleolus in many cases, but not in all. The protoplasm of the cells is so irregular in form as to give the impression that the cells are coherent in a sort of tissue, and not loosely arranged as in the lymphosarcoma. Mitotic figures are numerous and regular, and in many of the cells the nucleolus stains a pale, solid blue. Quite extensive areas of necrosis appear in some of the nodules. There are in places, especially in the nodules in the lymph glands, scattered lymphoid cells, among the typical tumor cells. The bronchial gland shows a distinct tumor nodule, of precisely the same type as is seen elsewhere. One bloodvessel or lymphatic vessel is found crowded with the tumor cells, and there are necroses in the tumor, but no tubercles. Section through the presacral pelvic peritoneum shows tumor nodules of the characteristic kind. In places the margins of these nodules show lymphoid cells, as if they had developed in small lymph glands. A section of the psoas muscle shows extensive tumor growth; it is interesting that the tumor frequently grows into the muscle fibers. This results in the isolation of the gland-like strands of tumor cells; otherwise the tumor has precisely the same character as seen elsewhere. The muscles about it are extremely atrophic and edematous. In one section in which the tumor invades the lymph gland near the aorta there is a good deal of necrosis, but through the necrotic areas there runs a bloodvessel, surrounded by mantles of the tumor cells, which are arranged radially in a distinctly perithelial type; elsewhere the tumor has the ordinary character. The tumor everywhere has a very highly invasive character.

In this case there were no leukemic changes and the bone-marrow shows only a response to the anemia. Nearly all the lymph glands are, however, enlarged by the presence of a growth which extends through their capsules, and mats them together, invading beyond into the muscle, bone, and subserous tissues, but scarcely involving the organs. In this way we have a sharply differentiated growth, easy to outline in the involved lymph glands, against the lymphoid structures, formed of a coherent tissue, composed of polygonal cells, and destroying instead of infiltrating the tissue into which it advances. It seems, therefore, that this has rather the character of a true sarcoma primary in the lymph glands than that of a lymphosarcoma.

Such a sarcoma may in some cases resemble even in its distribution the growths which we recognize as lymphosarcomata, but may be distinguished by its histological characters. Thus in the follow-



ing case, in which there was a large mediastinal tumor growing almost precisely as in Case VI of our series, the microscopic study revealed the histological structure of an alveolar sarcoma, possibly of endothelial origin.

Albert S., aged forty-five years; white; died January 2, 1898. (Autopsy No. 1037.)

*Anatomical Diagnosis.* Tumor of anterior mediastinum; alveolar sarcoma, possibly of endothelial origin; invasion of right lung along the bronchi; metastases in liver; cervical, anterior, and posterior mediastinal, gastrohepatic, parapancreatic, retroperitoneal lymph glands; acute and chronic pleurisy; chronic adhesive pericarditis; unresolved pneumonia.

*Body* is that of a well-built man. The superficial glands enlarged. The abdominal organs normally disposed. The liver extends 5 cm. below the costal margin. The gland in the gastrohepatic omentum enlarged, one the size of a pigeon's egg.

*Thorax.* The anterior mediastinal tissues are closely adherent to the sternum. The left pleural cavity contains 700 c.c. of turbid fluid. The right pleural cavity is obliterated by adhesions. About the pericardium there are some large solid glands. The upper portion of the mediastinum is occupied by a large mass which extends above the clavicles, and which depresses the heart. It is symmetrical and extends downward over the ascending and transverse part of the arch of the aorta, and over the anterior portion of the pericardium. It is very irregular in outline and is adherent to the left lung on its inner surface, and to the right lung over its upper portion, and has completely surrounded the large vessels at the root of the heart. It compresses the trachea, especially the right bronchus. The cut surface of the tumor has an alveolar appearance and is streaked with strands of fibrous tissue. The tumor is white, translucent, and soft, with points of opacity. It infiltrates the right lung along the branches of the bronchi, sometimes invading the bronchi. The posterior mediastinal and cervical glands are enlarged, and contain nodules of the same tissue. The left lung is not involved, but its surface is covered with fibrinous exudate.

*Heart* is bound in adhesion to the surrounding organs, but it is otherwise normal.

*Liver* weighs 2500 grams and contains 75 to 100 nodules, varying from the size of a pea to that of an egg. These have an alveolar structure, and are very soft, with many patches of necrosis. The superficial ones show an umbilicated appearance.

*Spleen* is large and soft, but contains no metastases. The other organs are practically normal, except for the *abdominal* and *retroperitoneal* glands, which show an infiltration with the new-growth, and are much enlarged.

*Microscopic Notes.* *Tumor.* The tumor tissue has a dense stroma of fibrous hyaline tissue, in the meshes of which there is a finer delicate reticulum, con-

taining some cells which are sometimes rounded, sometimes elongated. They have a vesicular nucleus with ragged cell body. In places there are very large cells with multiple nuclei, others with very deeply staining budded nuclei. In other places the cells are almost epithelial in appearance. In the liver nodules they are all elongated and show a distinctly alveolar arrangement. This tumor shows, thus, nothing of the adenoid structure and differs in many respects from the lymphosarcoma. It may be better regarded as an alveolar sarcoma.

The distinction which may be drawn between the true round-cell sarcoma and the lymphosarcoma depends not so much upon the histological characters of any isolated portion of the tumor as upon the determination of the point of departure of the growth, the manner of growth, and the manner of distribution.

In contrast with what has been written in describing the lymphosarcoma, we find the true round-cell sarcoma arising, not especially from lymphoid tissue, but from the connective tissue at any point, commonly from intermuscular tissues, periosteal, or subcutaneous tissues, etc., where it forms a mass which grows expansively, not from multiple or widespread areas of origin, but in one nodule, which infiltrates and destroys tissue in its advance. It is much less a characteristic of the true sarcoma than of the lymphosarcoma, to merely separate the elements of an invaded tissue, without bringing about their destruction, and it is, therefore, less common to find even remnants of the invaded tissue buried deep in the tissue of the sarcoma. The mode of growth is thus fairly distinctive in these two conditions. Metastasis takes place in true sarcomata, not so much by mere extension as by the rapid invasion of bloodvessels and the production of distant nodules, strictly according to the mechanical principles of the circulation. The involvement of even the draining lymph glands is sometimes lacking, but in other cases the glands are extensively affected. These are things which help to distinguish one form from the other rather better than the character of the cells and supporting tissue, which may show great similarity in the two.

On the whole it seems possible in this anatomical way to outline clearly enough the group of lymphosarcomata; it is only necessary, however, that this somewhat artificial classification be borne with patiently until the etiological factors become known, for then we shall see clearly:









